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St. Francis Hotel, San Francisco, California, June 22-25, 1950

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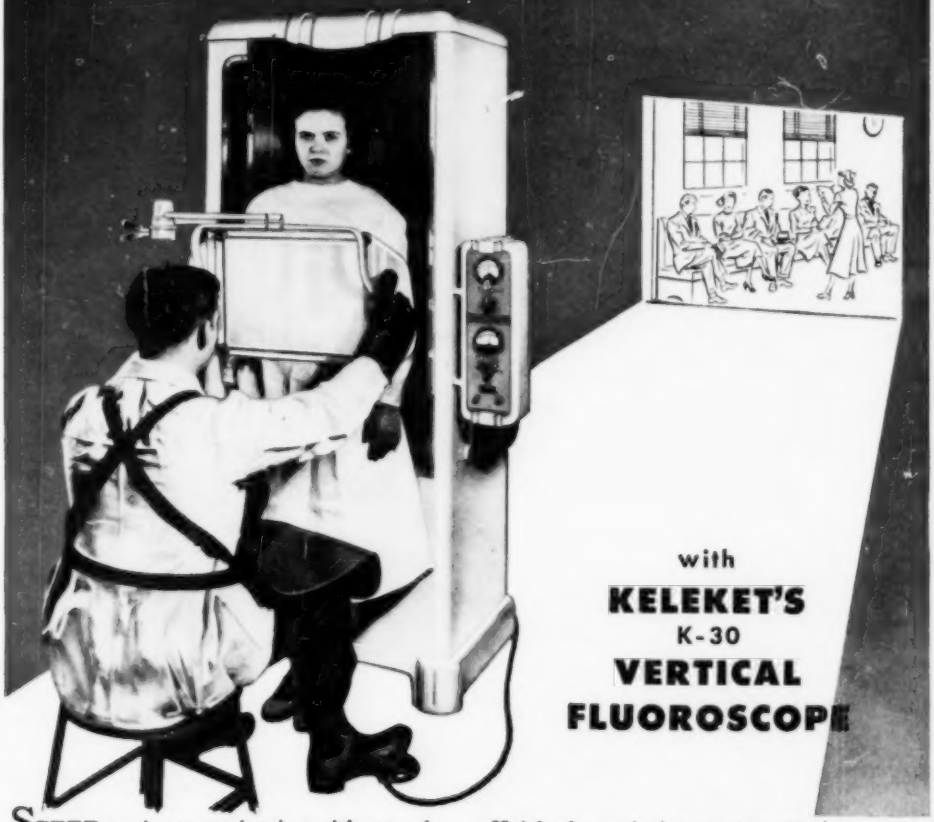

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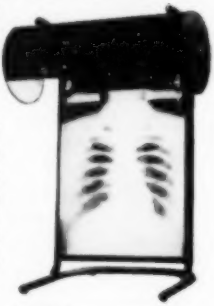

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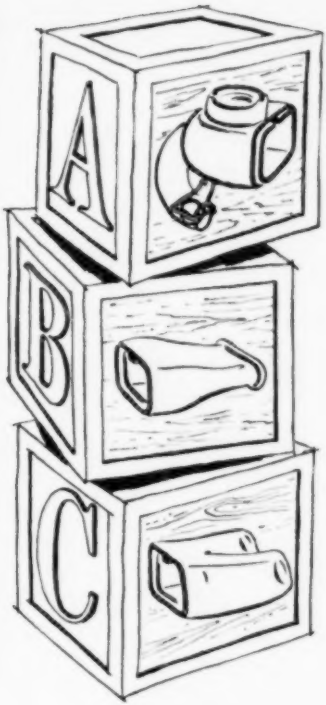

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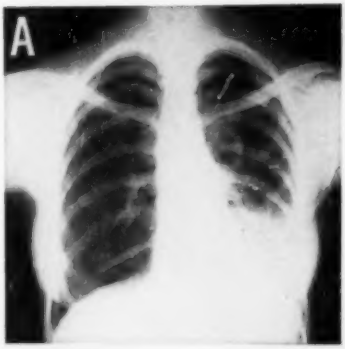

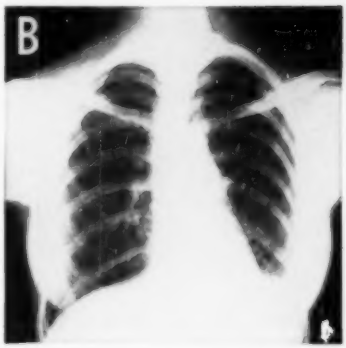

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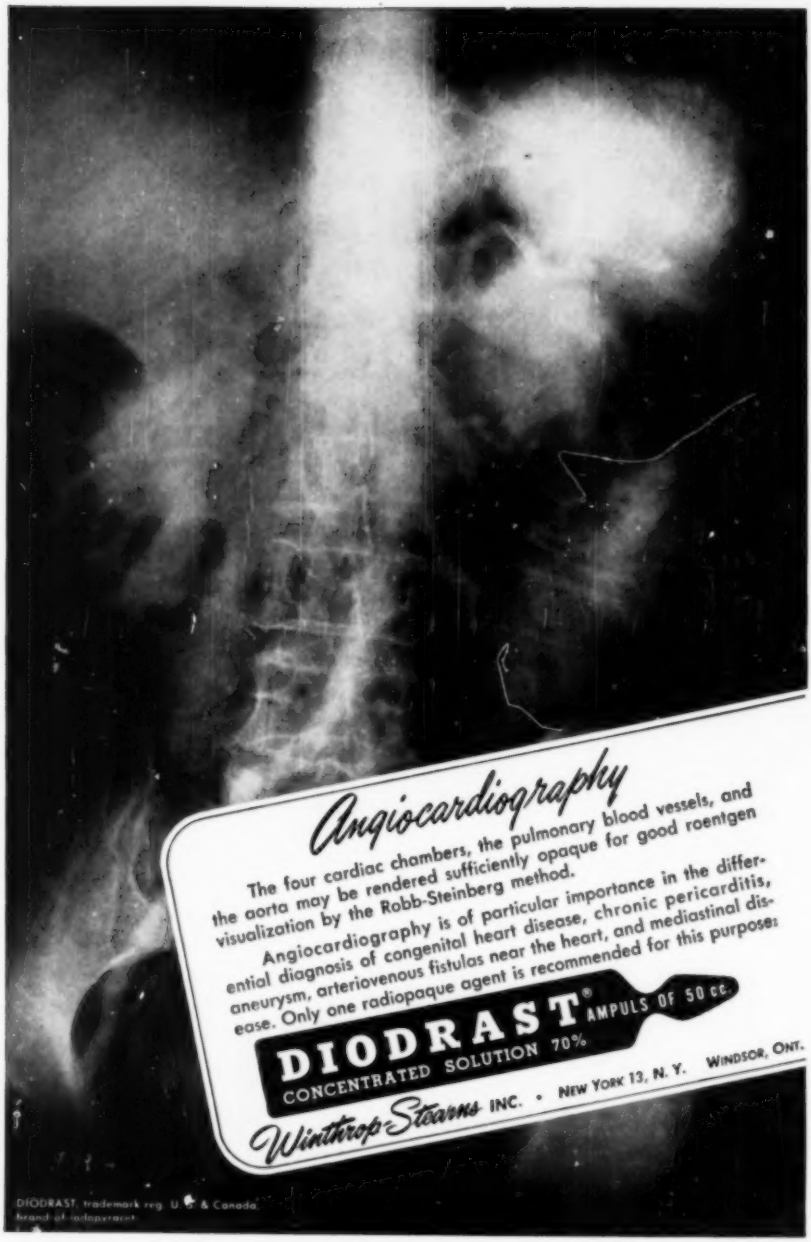
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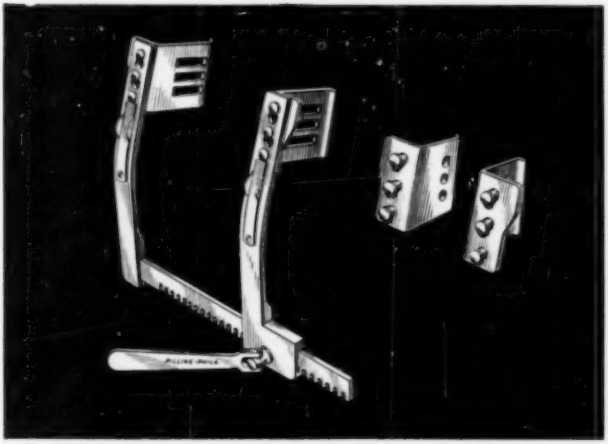

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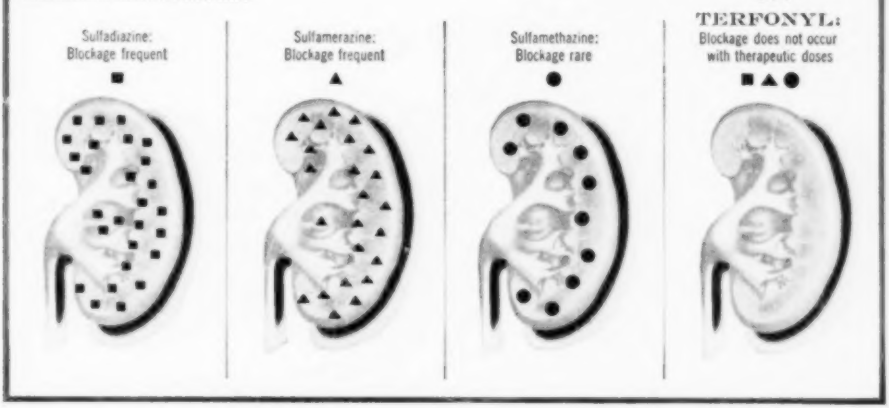

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DISEASES *of the* CHEST

VOL. XVII JANUARY 1950 NUMBER 1

Cytologic Diagnosis of Bronchogenic Carcinoma*

LEWIS B. WOOLNER, M.D.† and JOHN R. McDONALD, M.D.†
Rochester, Minnesota

With the development of thoracic surgery, accurate preoperative diagnosis of bronchogenic carcinoma has become increasingly important. It has been found that cytologic examination of sputum and bronchial secretions provides a useful adjunct to already established methods of diagnosis.[1-4]

Cytologic examination of sputum and bronchial secretions has been carried out in our laboratory for the past three years. During this time specimens from approximately 6,000 patients have been examined and a cytologic diagnosis of carcinoma has been made in more than 400 cases. Cytologic examination of sputum was the basis for the diagnosis in approximately four fifths of the total number; in the remaining cases the diagnosis was based on the examination of bronchial secretions, washings or smears made by direct swabbing of the bronchial wall.

Technic

In the collection of sputum for examination, patients are instructed to collect material actually coughed up and to avoid dilution with pharyngeal and nasal secretions. The sputum is collected in a few cubic centimeters of 95 per cent alcohol. Fresh sputum is somewhat easier to handle technically and is used for hospital patients when the time factor between collection of sputum and smearing of slides is not important. Five slides are made from each specimen and an attempt is made to examine three specimens from each patient. Bronchial secretions are brought to the laboratory and smeared directly. We have utilized the alcohol-ether fixation as described by Papanicolaou,[5] with hematoxylin-

*Presented at the 15th Annual Meeting, American College of Chest Physicians, Atlantic City, New Jersey, June 2 to 5, 1949.

†Division of Surgical Pathology, Mayo Clinic, Rochester, Minnesota.

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eosin stain. The slides are carefully scanned under low magnification, high dry magnification being used for cellular detail. In practice it has been found satisfactory to have the scanning procedure carried out by properly trained technicians, who mark suspicious cells or clumps for further study. Actual diagnosis is, however, always made by the pathologist. The time required for examination of slides varies. In a positive case in which many carcinoma cells are present, the examination may be completed in a few minutes. In a negative case in which all slides need to be carefully scanned, it may require 25 to 30 minutes, depending on the experience of the examiner. Smears are examined as complete unknowns and the results are reported positive or negative or, if an insufficient number of atypical cells is found to make a definite diagnosis, another specimen is called for.

We have found sputum and bronchial secretions to be of approximately equal value in the detection of carcinoma cells. Both have certain advantages and disadvantages. Bronchial secretions provide better localization and require somewhat less time for examination. Sputum examination, by virtue of the dilution factor, is more time consuming, but this is offset somewhat by the ease of obtaining additional specimens, a very important consideration when few cells are present in a given case and more evidence is required to make a definite positive diagnosis. We have found that an appreciable number of additional positive diagnoses of carcinoma may be made by the routine use of both sputum and secretions whenever possible.

The characteristics of exfoliated carcinoma cells as seen in various secretions have been adequately described.[6,7] In general, carcinoma cells are distinguished by their large cells, variation in size and shape of the cells, hyperchromatism of the nucleus and the presence of prominent nucleoli. Diagnosis is most readily made on the basis of clumps of exfoliated cells but equally accurate results can be obtained by finding a sufficient number of isolated single cells. Small-cell or "oat-cell" carcinomas are the most difficult to diagnose by the smear technic because of the small size of the cancer cells.

Care must be taken to distinguish immature phagocytes without pigment and clumps of squamatized bronchial epithelium from cancer cells.

Accuracy of Diagnosis

False Positive Diagnoses: It has been found that false positive diagnoses cannot be completely avoided in routine cytologic work. In our experience the false positive error has been approximately 2 per cent. In 400 cases in which a positive diagnosis of carcinoma

was made from smears of sputum or bronchial secretions there have been seven proved false positive reports. In an additional three cases, the clinical impression was not carcinoma but no follow-up on these patients has been obtained. In approximately 30 per cent of these 400 cases, tissue proof of the presence of carcinoma was not obtained. In the majority of these cases, however, the clinical and roentgenologic evidence of carcinoma was supported by such secondary evidence as metastasis to bone or enlarged lymph nodes, fixed vocal cord, pleural effusion, Horner's syndrome, superior vena caval obstruction or gross findings at bronchoscopic examination. In a few cases, the origin of the carcinoma cells was from the esophagus via a tracheo-esophageal fistula or from the upper part of the respiratory tract. In a small number, the lesion in the lung was assumed to be metastatic from a primary carcinoma elsewhere in the body. It has been our experience, however, that metastatic carcinoma does not regularly exfoliate cancer cells because of the somewhat infrequent bronchial involvement and because the mucosa tends to remain intact over the tumor.

False Negative Results: The presence or absence of cancer cells in a given case of bronchogenic carcinoma varies somewhat with the type and situation of the lesion. In general, tumors at the hilus or those involving large or medium-sized bronchi give a uniformly positive result. However, of tumors situated in the periphery, those for which no gross communication between the tumor and the bronchial tree can be traced will obviously give negative results. In a series of 588 patients with miscellaneous diseases of the thorax previously reported on by us,[5] a routine cytologic examination of sputum or bronchial secretions was carried out. Of this number, 147 patients were proved to have or were suspected of having bronchogenic carcinoma. In 100 of these, or 68 per cent of the total, a positive diagnosis of carcinoma was given by cytologic studies. This figure is probably lower than the true incidence since some of the false negative reports were based on an inadequate number of sputum examinations.

Value of Method as an Adjunct to Established Methods of Diagnosis: In our experience cytologic examination of sputum or bronchial secretions frequently gives positive results when the findings at bronchoscopic examination are negative or equivocal. In the series of 400 patients previously referred to, 144 underwent surgical exploration. Of this total, 79 (54.9 per cent) had a preoperative microscopic diagnosis of carcinoma on the basis of positive results obtained on bronchoscopic biopsy. In the remainder, positive smears provided the only preoperative microscopic evidence of malignancy. In 77 of these cases, pneumonectomy or

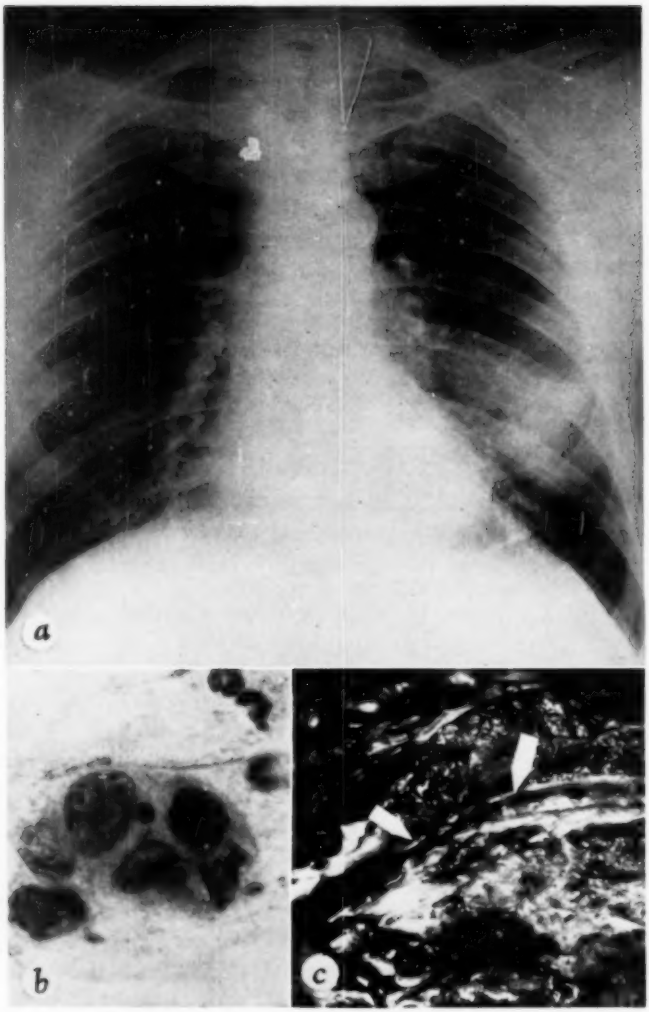

FIGURE 1: Bronchogenic carcinoma of the lingular division of the upper lobe bronchus. (a) Roentgenographic appearance. (b) Carcinoma cells found in sputum. (c) Gross lesion. The segment of bronchus involved measured 1.2 cm. in length. There was infiltration of the carcinoma through the entire thickness of the bronchial wall but not into the surrounding lung.

lobectomy was carried out, 45 of the operations being on the basis of positive results on biopsy and 32 on the basis of positive results obtained when smears were examined. To illustrate the type of case in which the results of sputum examination are positive and the results of bronchoscopic examination completely negative, the following case is cited.

A 64-year-old male came to the clinic for an examination. Four months before admission, he had had pain in the left side of the thorax. The pain extended down the arms and was thought to be on a cardiac basis. One month before admission, he had had a slight thoracic pain and an attack of influenza. He had had a slight cough with mucoid sputum but no hemoptysis. On admission, roentgenograms of the thorax revealed chronic pneumonitis with some reduction in volume of the lingular portion of the left upper lobe; no definite tumor was identified but the possibility of bronchogenic carcinoma or bronchiectasis was suggested (Fig. 1a). Bronchoscopic examination gave completely negative results. Secretions were removed for cytologic study but an insufficient number of atypical cells were found on which to base a diagnosis. The sputum, however, was positive for carcinoma cells (Fig. 1b). A diagnosis of bronchogenic carcinoma was thus made and a left pneumonectomy was carried out. A very small bronchogenic carcinoma, squamous type, was found surrounding the orifice of the lingular division of the left upper lobe bronchus (Fig. 1c). The lingular portion of the upper lobe distal to the carcinoma showed chronic pneumonitis. No lymph nodes were involved.

Value in the Diagnosis of Surgically Resected Bronchogenic Carcinomas

In an attempt to correlate the incidence of positive cytologic findings with the type and location of bronchogenic carcinoma, a group of 80 consecutive surgically removed bronchogenic carcinomas over a two-year period was studied. In this group, 40 were squamous-cell carcinomas, 20 were carcinomas of the large-cell type, 15 were adenocarcinomas and five were carcinomas of the small-cell or "oat-cell" type. In the 80 cases bronchoscopic biopsy gave positive results in 38 or 47.5 per cent. Sputum or bronchial secretions were examined in 73 of these cases and positive results were reported in 51, or 70 per cent. By combining the two methods, a positive preoperative microscopic diagnosis of carcinoma was made in 59 out of 80 cases, or 73.8 per cent.

Squamous-cell Carcinoma: Squamous-cell carcinoma is the most frequent histologic type of bronchogenic carcinoma. There is a marked tendency for it to involve the larger bronchi; hence the cytologic findings are usually positive. Of the 40 patients with squamous-cell carcinomas in this group, 35 had cytologic examinations, in 28 (80 per cent) of whom positive results were reported. Of the seven cases in which cytologic examination gave negative results, the biopsy gave positive results in two. In all cases there

was at least some degree of gross bronchial involvement by the tumor.

Large-cell Type: Of the 20 patients with large-cell carcinomas, 19 were examined cytologically, in 12 (63.2 per cent) of whom positive results were reported. Of the seven cases in which cytologic examination gave negative results, the lesion in one was peripheral, in two it involved a very small bronchus, in one it was cavernous or cystic and was situated in the upper lobe and in three it involved fairly large bronchi.

Adenocarcinoma: Adenocarcinoma is probably the least frequent histologic type of bronchogenic carcinoma. It tends to be more peripheral in situation frequently forming a subpleural nodule to which no direct bronchial communication can be traced. Histologically it may be impossible to differentiate such tumors from metastatic adenocarcinoma. In this series all 15 of the patients with adenocarcinoma were examined cytologically. In only eight of the 15 were there positive findings (53.3 per cent). Of the seven cases in which cytologic studies gave negative results, the lesion in four was subpleural with no demonstrable bronchial involvement, in two it was peripheral with minimal ulceration of a bronchus and in one it was a peripheral nodule which was possibly metastatic from an ovarian carcinoma removed four years previously. Of the eight cases of adenocarcinoma in which cytologic

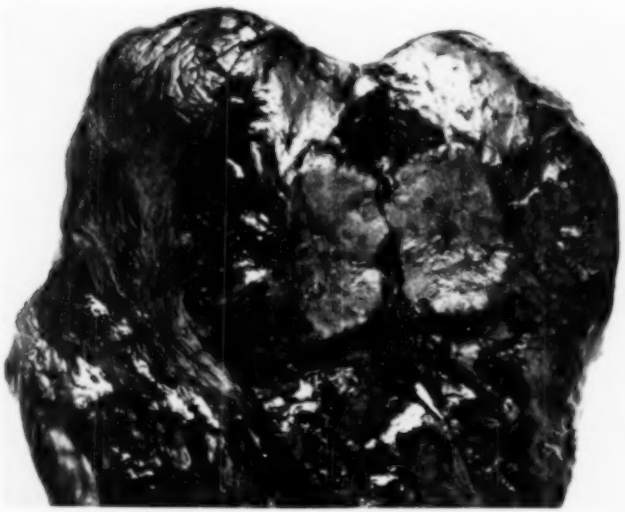

FIGURE 2: Peripherally placed bronchogenic carcinoma. The sputum examination gave negative results in this case.

studies gave positive results, in only one was the lesion peripherally situated, the lesion in the remainder involving the major bronchi or one of the moderate-sized subdivisions. It is apparent that there is a group of cases of peripherally situated carcinomas frequently of the adenocarcinoma type in which no, or very minimal, communication with the bronchial tree can be traced and in which the cytologic findings will be fairly consistently negative. Of the lesions in the 80 cases of bronchogenic carcinoma in this series, eight or 10 per cent, were peripheral and no communication could be traced between the tumor and the bronchial tree. In a recent case, such a carcinoma was found at operation in spite of the fact that 15 consecutive sputum examinations had been carried out with negative results (Fig. 2). In some peripheral bronchogenic carcinomas, however, the tumor communicates with a moderate sized bronchus and carcinoma cells may be found in the sputum. One such tumor is shown in Figure 3.

Small-cell Group: Small-cell bronchogenic carcinomas are the least frequent in a surgical series because of their rapid growth and widespread early metastasis. In this series only five were of the small-cell type, and three of these out of four cases examined were associated with sputum or bronchial secretions that were positive for carcinoma cells (75 per cent). In our experience patients with these tumors show consistently positive cytologic findings in keeping with the tendency of such tumors to involve the larger bronchi.

FIGURE 3: Peripherally placed bronchogenic carcinoma. There was gross bronchial involvement by the tumor in this case and sputum examination gave positive results.

Alveolar-cell Tumor: Our experience with alveolar-cell tumors has been based on seven surgically removed specimens. It is difficult to establish a preoperative diagnosis of tumors of this type. The symptoms are nonspecific although voluminous mucoid or watery sputum may be noted. The bronchoscopic examination gives consistently negative results and the roentgenogram of the thorax may simulate sarcoidosis or other inflammatory conditions. On five of the patients with this type of tumor, cytologic examination was carried out preoperatively. The sputum was positive for carcinoma cells in three, equivocal in one and negative in one. It would appear that the findings of atypical cells in the sputum may aid considerably in the preoperative diagnosis of alveolar-cell tumor.

Adenoma and Cylindroma: Adenoma and cylindroma constitute possibly 5 per cent of primary pulmonary neoplasms but a somewhat larger portion of surgically removed pulmonary tumors. Because of the intact mucosa over the surface of the tumor, the cytologic findings in this group have been consistently negative. The findings of carcinoma cells in the sputum may aid considerably in the differential diagnosis between adenoma and "oat-cell" carcinoma.

SUMMARY

Our experience with cytologic diagnosis of bronchogenic carcinoma has been summarized. To date in more than 400 cases of bronchogenic carcinoma the diagnosis has been made cytologically with a false positive error of approximately 2 per cent. In our experience the false negative error has been approximately 30 per cent. Of 80 consecutive surgically removed bronchogenic carcinomas, 10 per cent were peripherally placed showing slight or no gross communication with the bronchial tree. Cytologic examination in the case of these peripherally located tumors gave negative results. Cytologic studies are of value in the diagnosis of alveolar-cell tumor but of no value in bronchial adenoma or cylindroma.

RESUMEN

Se ha resumido nuestra experiencia en el diagnóstico citológico del carcinoma broncogénico. Hasta ahora en más de 400 casos de carcinoma broncogénico, se ha hecho el diagnóstico citológico con error de falsos positivos aproximadamente de 2 por ciento. En nuestra experiencia el error por falsos negativos ha sido de 30 por ciento. De 80 carcinomas broncogénicos quirúrgicamente extirpados, 10 por ciento estaban ubicados periféricamente mostrando muy pequeña o ninguna comunicación con el árbol bronquial. El examen citológico de estos tumores periféricos dió resultados nega-

tivos. Los estudios citológicos son de valor en el diagnóstico en el tumor de células alveolares, pero no tienen valor en el diagnóstico del adenoma bronquial o en el del cilindroma.

REFERENCES

1 Dudgeon, L. S. and Wrigley, C. H.: "On the Demonstration of Particles of Malignant Growth in the Sputum by Means of the Wet-film Method," *J. Laryng. and Otol.*, 50:752, 1935.
2 Herbut, P. A. and Clerf, L. H.: "Bronchogenic Carcinoma: Diagnosis by Cytologic Study of Bronchoscopically Removed Secretions," *J.A.M.A.*, 130:1006, 1946.
3 Papanicolaou, G. N.: "Diagnostic Value of Exfoliated Cells from Cancerous Tissue," *J.A.M.A.*, 131:372, 1946.
4 Woolner, L. B. and McDonald, J. R.: "Symposium on Identification of Carcinoma Cells in Sputum, Bronchial Secretions and Urine. Bronchogenic Carcinoma: Diagnosis by Microscopic Examination of Sputum and Bronchial Secretions; Preliminary Report," *Proc. Staff Meet., Mayo Clin.*, 22:369, 1947.
5 Papanicolaou, G. N.: "A New Procedure for Staining Vaginal Smears," *Science*, 95:438, 1942.
6 Wandall, H. H.: "A Study on Neoplastic Cells in Sputum as a Contribution to the Diagnosis of Primary Lung Cancer," *Acta chir. Scandinav.*, 91 (Suppl. 93):1-143, 1944.
7 Woolner, L. B. and McDonald, J. R.: "Carcinoma Cells in Sputum and Bronchial Secretions; A Study of 150 Consecutive Cases in Which Results were Positive," *Surg., Gynec. and Obst.*, 88:273, 1949.
8 Woolner, L. B. and McDonald, J. R.: "Cytologic Diagnosis of Bronchogenic Carcinoma," (In press).

Discussion

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It is the opinion of Dr. Clerf and myself that cytological examination of bronchoscopically removed secretions is scientifically more accurate and clinically more rewarding than examination of sputa. We have no doubt that a diagnosis of bronchial carcinoma can be made by examining the sputum, but the purpose of this whole procedure is to arrive at an "early" diagnosis of cancer and everybody knows that early in the course of the disease there is no sputum available. In fact our best results are in those cases in whom the bronchial segment is gingerly washed with saline—a step that is necessary when there are no secretions available even at the time of bronchoscopic examination. If neoplastic cells are found in sputum a bronchoscopic examination must be performed to determine the location of the tumor and the operability. If, on the other hand, neoplastic cells are not found in the sputum and the patient is suspected of having cancer a bronchoscopic examination must also be performed. Therefore, why not do it in the first place?

Our results as of May 26, 1949, are as follows: In a total of 307 cases of cancer of the lung neoplastic cells were found in bronchoscopically removed secretions in 272 or 88.6 per cent. A bron-

choscopic biopsy was possible in 104 of the cases or 33.8 per cent. Indirect evidence of tumor in the form of stenosis, fixation, etc., was present in 87 cases. Neoplastic cells were present in secretions and bronchoscopic examination was entirely negative in 94 cases or 30.6 per cent. It might be of interest also to correlate the bronchoscopic findings with the stage of the disease. In a consecutive series of 69 total pneumonectomies performed by Dr. Gibbon bronchoscopic examination was completely negative in 25, and in 18 of these neoplastic cells were present in the secretions. In only two of these 25 cases were there metastases to the peribronchial and mediastinal lymph nodes. In 44 cases in which there was bronchoscopic evidence of tumor (positive biopsy in 21 and deformity, etc., in 23) neoplastic cells were present in secretions in 39 cases. In 23 of these 44 cases the tumor had already spread to the draining lymph nodes.

In conclusion, I heartily concur with Dr. McDonald that cytologic diagnosis of cancer of the lung is an extremely valuable adjunct in the fight against this disease. I am sure the procedure is here to stay.

SEYMOUR M. FARBER, M.D., F.C.C.P.
San Francisco, California

This has been a most interesting and important report in the cytologic field. Unfortunately there are very few groups where careful statistics have been kept of the attempts to find malignant cells in the sputum and bronchial secretions of patients. Doctor McDonald's analysis of his experience in a diagnostic center reveals the importance of these studies.

We have been accepting specimens at the University of California from various medical schools, teaching and private hospitals, veterans administration hospitals, tuberculosis sanatoria and from private physicians. Specimens from 1243 patients were submitted and in this group there were 319 patients who had malignant pulmonary disease. When five or more sputum specimens were submitted, 88 per cent of the proved cases of bronchogenic carcinoma were diagnosed by cytologic methods. When only one specimen was submitted or when incomplete sputum studies were offered for examination, we were able to diagnose 61 per cent of the proved cases.

There is very little that one can add to the excellent presentation of Doctor McDonald except to indicate again a warning. The reliability and the sensitivity of the cytologic technique can be readily obtained by competent cytologists, but it must be remembered that the reliability in particular requires experience.

Bed Rest, Collapse, and Streptomycin in the Treatment of Pulmonary Tuberculosis*

I. Clinical and Roentgenologic Observations

(A Preliminary Report)

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Introduction

In the Spring of 1947 the U. S. Naval Hospital at St. Albans, New York became the tuberculosis center for the Naval Medical Department in the eastern half of the United States. Since that time the tuberculosis service of this hospital has grown to a census of 280 patients, the average monthly admission rate being about 30 cases. During the period covered by this report, (January 1947 to June 1948), 440 cases of pulmonary tuberculosis have been observed and treated.

We have reviewed 77 cases treated with streptomycin on whom adequate data could be accumulated by means of follow-up letters in cases discharged to Veterans Administration Hospitals and by review of protocols made up for each case. These protocols comprised reproductions of representative chest roentgenograms, a graphic record of the highest temperature for each week of hospitalization, a tabulation of the weight, daily sputum production, monthly sedimentation rate, status of the sputum or gastric contents on smear and culture, and recording of the various methods of treatment used.

Most of the studies published to date on streptomycin in the treatment of pulmonary tuberculosis[1-15] have limited the reported cases to those which received no collapse therapy during the observation period in order that the results obtained with streptomycin alone might best be evaluated. The concensus expressed was that streptomycin constituted a valuable adjunct, but was not capable of adequately treating the majority of cases unless other therapeutic measures were applied. Most of these reports

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state that a program of bed rest plus collapse therapy integrated with streptomycin administration will best delineate the potentialities and limitations of streptomycin. This paper constitutes a preliminary report describing the early results obtained by such a program.

Material

The characteristics of the streptomycin treated group are listed and contrasted to the tuberculosis service as a whole in Table 1. Several interesting differences between the two groups are apparent.

Negroes, with their tendency to develop exudative type lesions, required streptomycin relatively more frequently than whites. Streptomycin-treated cases received collapse therapy more often than the remainder of the service, but bed rest was frequently the only other therapeutic method used. In time an even larger percentage of the streptomycin-treated cases will receive collapse measures because 15 of the cases have been followed for three months or less.

Since Naval Personnel are subject to routine chest roentgenograms, we were interested in seeing the relationship that existed between mass surveys and streptomycin therapy. Half of our total group of patients were admitted to the hospital because of findings on routine chest roentgenograms; yet 85 per cent of the streptomycin-treated group were admitted because of symptoms.

All members of the group were males and presumably in good health upon entry into the Navy. Almost half (43 per cent) of the streptomycin-treated group are known to have had negative chest photofluorograms two years or less prior to the diagnosis of pulmonary tuberculosis.

All cases had positive cultures of the sputum or gastric contents to establish the diagnosis.

Methods

Early in the period covered by this report the average dosage of streptomycin was three grams per day. This was gradually reduced to one gram per day by July of 1947. The drug was administered in four divided doses until recently when it was given twice daily. In every instance it was given intramuscularly. Fourteen cases were begun on streptomycin in other hospitals, and the majority of these patients received large daily doses. If it was decided to continue treatment, the dosage was reduced to one gram daily. Thus we have given 1.0 to 1.9 grams per day to 69 cases, five have been given 2.0 grams to 2.9 grams, and two received 3.0 to 4.0 grams daily.

Originally these dosages were given for prolonged periods which were frequently as long as three, four, or even five months. Since July, 1947 a course of streptomycin has been limited to not more than six weeks, but several patients have received more than one course. This schedule of one gram daily for six weeks has been followed in 63 instances.

The cases have been seen in conference with all members of the tuberculosis staff soon after admission to the hospital, and prior to any change in therapy. If the decision of the conference

TABLE 1

		Streptomycin Group	Per cent	Remainder of Service	Per cent
AGE:	17 - 20	25	32	95	26
	21 - 30	38	50	174	48
	31 - 40	10	13	59	16
	41 - 50	4	5	23	6
	51 - 60			11	3
	61 - 70			1	
	Total:	77		363	
RACE:	White	52	67	319	88
	Negro	20	26	33	9
	Filipino	5	7	11	3
ANATOMIC EXTENT OF DISEASE:					
	Minimal		5		32
	Moderate		30		34
	Far Advanced		65		34
REASON FOR ADMISSION:					
	Routine Film		14		57
	Symptoms		86		43
FEBRILE ON ADMISSION (100°)			68		7
TREATMENT:					
Pneumothorax		18		49	
Pneumothorax plus thoracoplasty		7		14	
Primary thoracoplasty		5		11	
Phrenic and Pneumoperitoneum		10		25	
Resection		4		6	
Bed rest		33		259	

TABLE 2 — CLASSIFICATION AND CHARACTERIZATION OF ALL CASES

No. of Cases	Collapse	Sputum Neg. 6 Months	N.T.A. Classification	Results on Cases Available for "Jury" Review 1. X-Ray (+) (0) (−)	2. Clinical (+) (0) (−)	3. Over-all (+) (0) (−)
ACUTE PULMONARY TUBERCULOSIS						
Tuberculous Lobular Pneumonia Without Cavitation						
6	None 4 Pnx 2	2	A.A. 1 Q. 1 Act. 4	4 0 0	4 0 0	4 0 0
Tuberculous Lobular Pneumonia With Cavitation (Moderately Advanced)						
20	None 10 Pnx 5 Thor 4 PpP 3	5	A.A. 0 Q. 5 Act. 15	10 3 0	11 2 0	9 4 0
Tuberculous Lobular Pneumonia With Cavitation (Far Advanced)						
22	None 4 Pnx 7 Thor 4 PpP 7 Res 1	2	A.A. 0 Q. 2 Act. 20 Dead 1	9 5 2	9 5 2	2 14 0
Confluent Tuberculous Lobular Pneumonia (Tuberculous Pneumonia)						
19	None 4 Pnx 9 Thor 4 PpP 1 Res 3	6	A.A. 1 Q. 5 Act. 13 Dead 2	9 1 2	10 0 2	8 4 0
SUBACUTE PULMONARY TUBERCULOSIS (Fibro-Caseous and Fibro-Cavernous)						
5	None 5	0	Act. 5	3 0 0	3 0 0	3 0 0
MISCELLANEOUS						
4	None 4	1	Q. 1 Act. 3	3 0 0	3 0 0	2 1 0

TUBERCULOUS EMPYEMA

No. of Cases	Type of Fluid	Bacteriology	Obliteration of Space By:			
5*	Turbid 2 Purulent 3	Pos. for M. Tuberc. 5	Re-expansion of Lung Thoracoplasty Resection of Lung	1 2 2	Empyema Quiescent Follow-up Inadequate Dead	3 1 1

*(2 cases included in Tuberculous Pneumonia Group)

LEGEND:
Pnx — Pneumothorax
Thor — Thoracoplasty
PpP — Phrenic and Pneumoperitoneum
Res — Resection
A.A. — Apparently Arrested
Q. — Quiescent
Act. — Active

was at all controversial, the case was taken to a medical-surgical conference attended by the civilian consultants in thoracic medicine, thoracic surgery, and pathology.

In evaluating these patients the following points were considered when deciding whether streptomycin was indicated:

1. Elevation of temperature, pulse, and sedimentation rate.
2. Recent onset of disease as judged by the history and serial chest roentgenograms taken prior to admission.
3. Predominantly exudative type disease judged roentgenographically.
4. Symptoms indicative of toxemia such as malaise, anorexia, etc.
5. Failure of above manifestations to improve on bed rest.

It was our intention to withhold streptomycin from new admissions for at least six weeks in order that the effect of bed rest alone on the clinical course of the disease could be determined. In the event that the drug had been used in another hospital, this program would obviously be impossible. If the indications were sufficiently urgent, i.e. (tuberculous pneumonia, tuberculosis meningitis), streptomycin therapy was begun immediately. The drug was rarely used if it seemed likely that good results could be expected without it. The administration of the drug was deferred in the event that excisional surgery was planned in the future. This hesitancy to use streptomycin was due to our fear that bacterial fastness would develop, thereby depriving the patient of its value in the future when it might be strongly indicated.

We realize that a prejudice existed in our minds toward the results obtained in these cases. Accordingly, a "jury" of experienced men* — one phthisiologist, one pathologist, and one thoracic surgeon have reviewed a number of the clinical histories, chest films, and protocols. They were asked to decide whether:

1. The roentgenograms showed evidence of improvement in the lesions following streptomycin therapy.
2. There was over-all clinical improvement in the patient.
3. The combination of 1 and 2 was greater than could be expected without streptomycin.

In Table 2 these opinions are tabulated with a (+) meaning yes, a (0) meaning no change, and a (−) meaning no.

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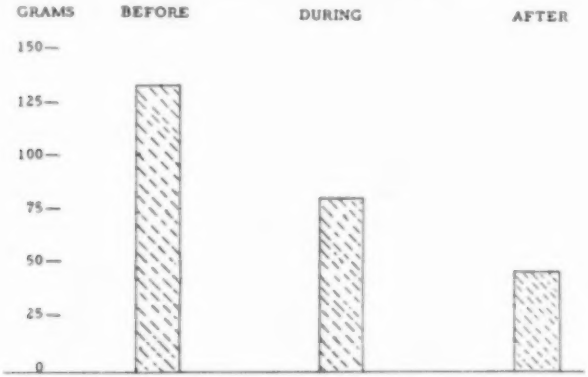
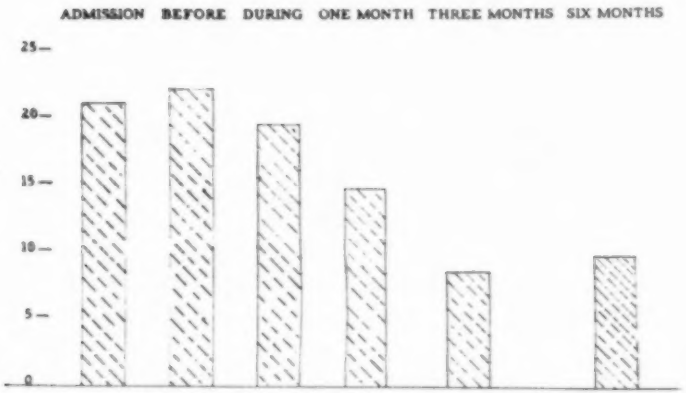
Clinical Results

The cases studied have been divided into seven pathologic types, and the clinical, roentgenologic and bacteriologic response to streptomycin therapy has been studied in each category. In Table 2, which classifies the patients studied, we have recorded the number of patients in each group, the type(s) of collapse therapy used, the status of the sputum at the time of writing (June 1948), and the result of the "jury" review.



AVERAGE DAILY SPUTUM PRODUCTION IN 35 PATIENTS ESTIMATED FOR THE MONTH PRIOR TO, THE MONTH DURING AND THREE MONTHS FOLLOWING STREPTOMYCIN

CHART 1



AVERAGE SEDIMENTATION RATE IN 57 PATIENTS ON ADMISSION, BEFORE, DURING, ONE, THREE, AND SIX MONTHS AFTER RECEIVING STREPTOMYCIN

CHART 2

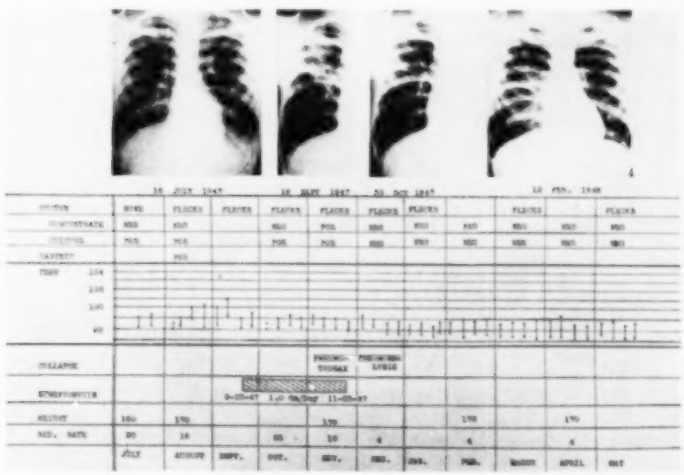
The quantity of sputum produced per day by 37 patients on whom data was available is recorded for the period prior to, during, and following streptomycin therapy in Chart 1. The changes in the sedimentation rate before, during, and after streptomycin treatment is shown in Chart 2. All cases lost weight prior to entering the hospital. Weight gain was minimum while hospitalized prior to receiving streptomycin, and the majority (56 per cent) gained an average of 11 pounds following treatment.

Acute Pulmonary Tuberculosis

Tuberculous Lobular Pneumonia Without Cavitation; This group consists of six cases in which spread of disease indicated streptomycin therapy. Four of these patients were treated with bed rest alone, and two received artificial pneumothorax. Of the four reviewed by the "jury" all received three pluses. Case 1 is an example of this type of disease and its response to treatment.

J.D., an 18 year old Negro, was admitted to the hospital because of findings on a routine chest roentgenogram. He was treated initially with bed rest, but on this regime developed an acute spread of disease with fever to 101 degrees F. and for the first time a positive sputum was found.

He was given one gram of streptomycin daily for two months. The temperature became normal, pneumothorax was induced and subsequently pneumonolysis was performed. The remainder of the hospital course was uneventful, and he was discharged to the Veterans Administration for rehabilitation.



CASE 1

Tuberculous Lobular Pneumonia With Cavitation (Moderately Advanced); The various procedures used in addition to bed rest and streptomycin for treating this group of patients are shown in Chart 3. In 13 cases reviewed by the "jury" nine responded better than expected, and five were quiescent according to National Tuberculosis Association classification. Chart 4 demonstrates the temperature response of this group. Case 2 is an example.

F.B., a 20 year old Negro, was admitted to the hospital because of findings on a routine chest roentgenogram. Questioning revealed a 16 pound weight loss and the presence of cough productive of 15 cc. of mucopurulent sputum daily.

Initially, treatment consisted of bed rest, but because of persistent fever one gram of streptomycin was given daily for six weeks. Since the sputum became negative on smear and culture, and since the lost weight was rapidly regained collapse therapy was not instituted. He was discharged to the Veterans Administration for rehabilitation.

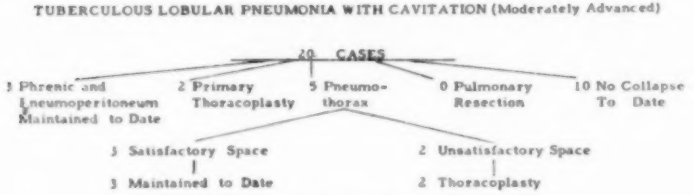
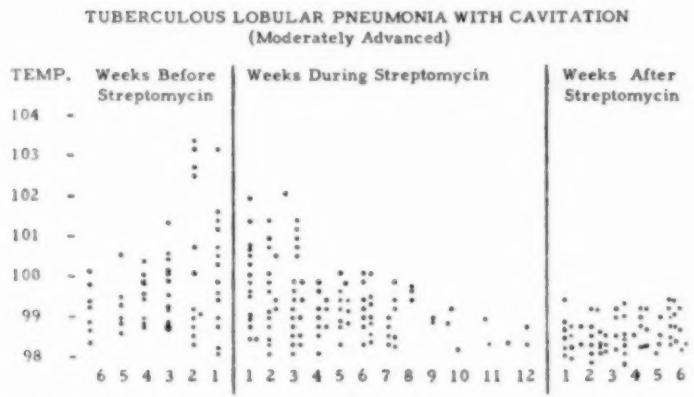
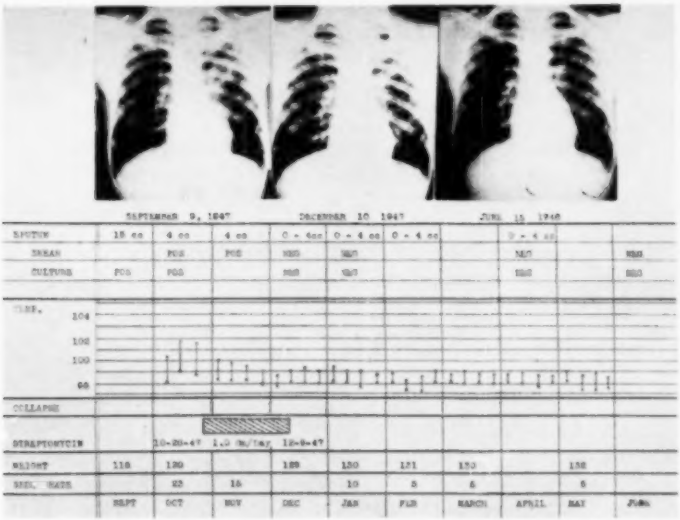


CHART 3



Highest Weekly Temperature for the Six Weeks Prior To, The Weeks During, and the Six Weeks Following a Course of Streptomycin

CHART 4



CASE 2

Tuberculous Lobular Pneumonia With Cavitation (Far Advanced); Charts 5 and 6 demonstrate the modes of treatment employed and the temperature response for this group. From Table 2, it will be noted that in 16 cases reviewed by the "jury" only two had improved more than was expected. In spite of these unfavorable findings, 14 cases were prepared for collapse therapy which would have been contraindicated in most had streptomycin been unavailable. Case 3 is an example of this group which was prepared for thoracoplasty.

W.P., a 30 year old Negro, was admitted to the hospital because of a "chest cold." Subsequent investigation revealed the presence of positive sputum, and the roentgenogram reproduced. Because of the febrile course

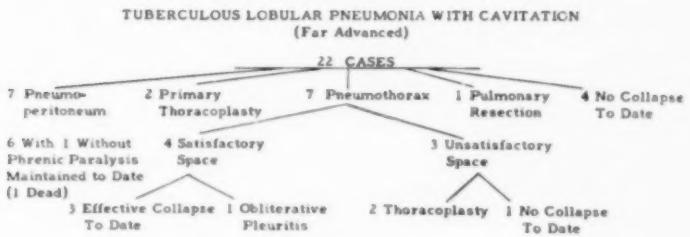
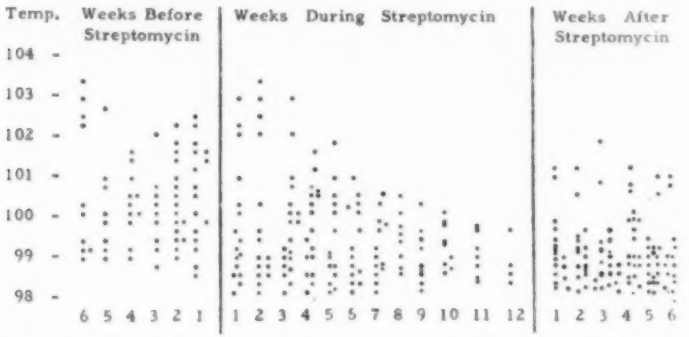


CHART 5

and the evidence of contralateral disease, he was given streptomycin for 14 weeks. The temperature became normal, the lost weight was partially regained, and the disease in the contralateral lung stabilized. Thoracoplasty was done in three stages.

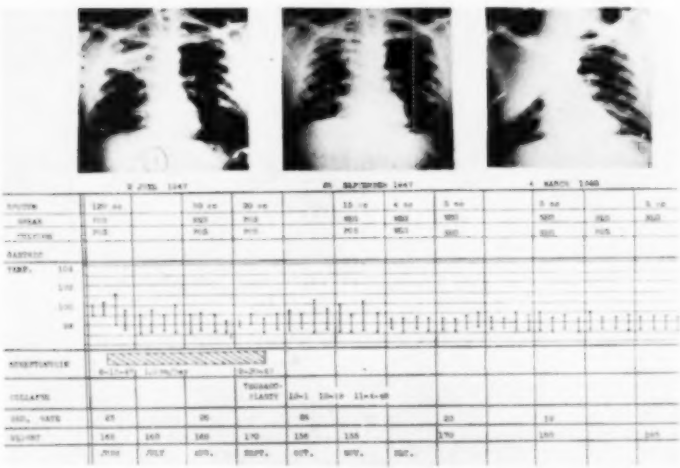
The sputum became negative except for positive cultures in the fifth postoperative month, and the contralateral disease remained under control. He was discharged to the Veterans Administration for rehabilitation.

TUBERCULOUS LOBULAR PNEUMONIA WITH CAVITATION (Far Advanced



Highest Weekly Temperature for the Six Weeks Prior To, The Weeks During, and the Six Weeks Following a Course of Streptomycin

CHART 6



CASE 3

Confluent Tuberculous Lobular Pneumonia

This entity, usually known as tuberculous pneumonia, was observed in 19 cases. The methods of treatment are shown in Chart 7, and the temperature curve for the group is demonstrated in Chart 8. Twelve cases were reviewed by the "jury" and eight were found to be benefited by streptomycin therapy more than could be expected. Five individuals had negative sputum at the date of writing. Although the observation period is short, the results differ markedly from those reported by Shields,[16] prior to the advent of streptomycin therapy. This group is represented by Case 4 whose course was uncomplicated, and by Case 6 who developed tuberculous empyema.

J.D., a 19 year old Negro, was admitted to the hospital because of sudden onset of chest pain, chills, fever, and non-productive cough. The

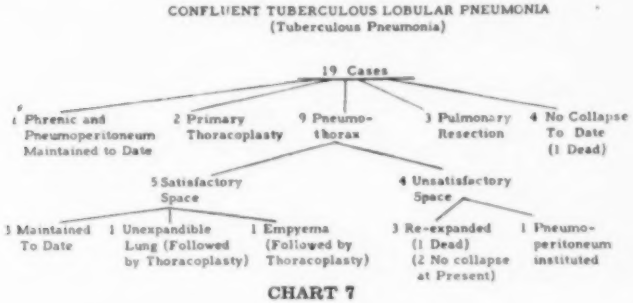
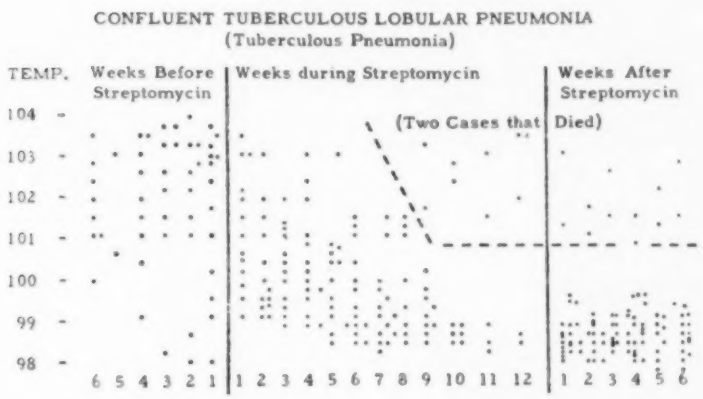


CHART 7

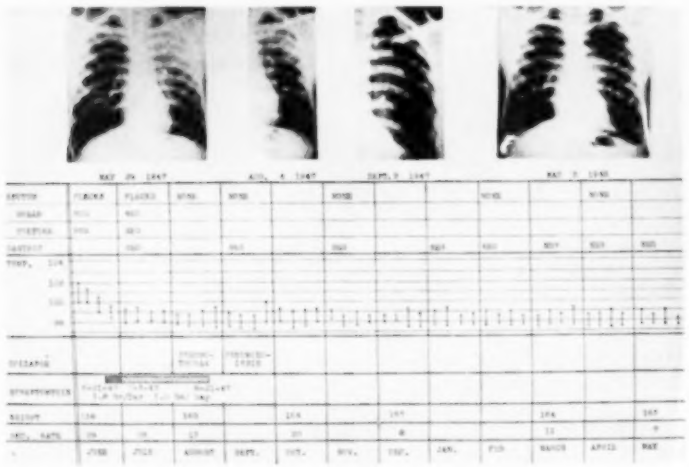


Highest Weekly Temperature For The Six Weeks Prior To, The Weeks During And The Six Weeks Following A Course Of Streptomycin.

CHART 8

chest roentgenogram revealed evidence of consolidation of the left upper lobe, and the sputum was positive on smear for acid fast bacilli.

Because of the massive involvement, and the high fever, he was given 1.8 grams of streptomycin daily for 10 days, and 1.2 grams daily for an additional 50 days. During this period the temperature became normal and the sputum converted. Artificial pneumothorax was induced and subsequently pneumonolysis was performed. The remainder of the hospital course was uneventful, and he was discharged to the Veterans Administration for out-patient care.



CASE 4

Sub-Acute Pulmonary Tuberculosis

Fibro-Cavernous and Fibro-Caseous Disease: There were five middle aged men in this series who had recently developed clinically active pulmonary tuberculosis. The tendency for males in this age group to react thus is evident from a study of the mortality tables,[17] and in recent years attention has been directed to the clinical aspects of this phase of pulmonary tuberculosis[19-21]. Howlett and O'Conner[22]have recently described the response of this type of case to streptomycin therapy, and they employ the term "grumblers" to describe the patients.

Since it is likely that individuals in this age group will spend the remainder of their lives harboring active pulmonary tuberculosis, there is a definite hazard in giving them streptomycin. Should their organisms become resistant to the drug, and should they transmit disease to their associates or to hospital personnel, the value of streptomycin could never be realized by these contacts. Recognizing the potentialities of this hazard, we have,

nevertheless, considered the indications sufficiently strong in five cases to give them the drug with the understanding that they would not leave the hospital unless their disease should become arrested.

The first case in this group was especially gratifying, and the results obtained prompted us to use streptomycin in other similar patients.

D.S.P., a 43 year old Brazilian with diabetes mellitus, had been hospitalized for over two years in the United States. During this period he had lost weight constantly and remained febrile to 102 and 103 degrees. He was anxious to return to Brazil, but in November of 1947 had several massive hemoptyses. These ceased spontaneously, but the fever persisted. Streptomycin was given because of the remote possibility that it might be of sufficient benefit to enable him to return to Brazil inasmuch as transportation facilities were available for the first time since the end of the war. After six weeks of treatment with one gram of streptomycin daily, the temperature decreased to a 99 degree range, he gained 13 pounds, his appetite returned, and he stated that he felt better than at any time during the past several years. However, there was no regression of the lesions noted on the chest roentgenograms. The trip home was made with no untoward effects.

The remaining four cases are similar, but they have been followed for longer periods since discontinuing streptomycin therapy. All have had a surprising decrease in fever, a moderate weight gain, an increase in feeling of well-being, and cough and sputum have decreased. Case 5 is a typical example of this group.

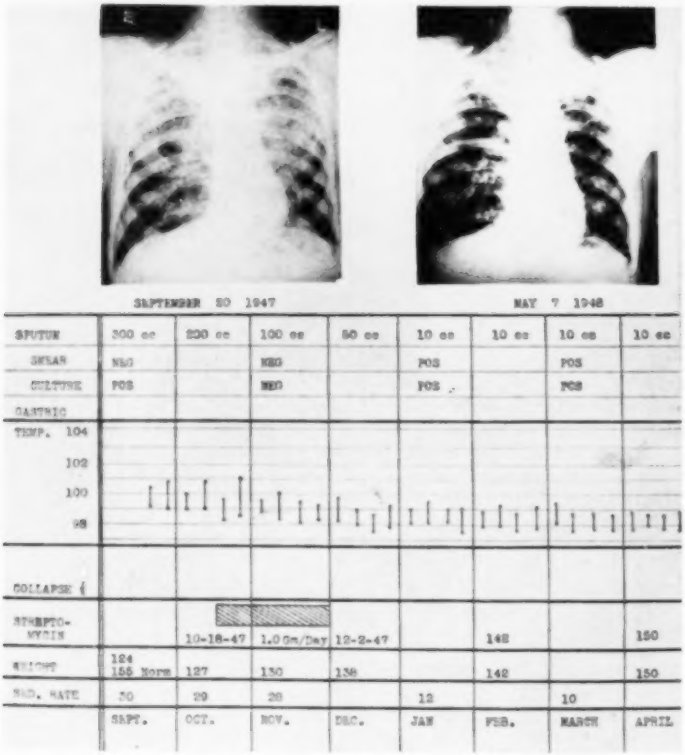
J.R., a 38 year old white man, was admitted to the hospital because of findings on a routine chest roentgenogram. He stated that he had lost 30 pounds during the preceeding six months, but attributed this to overwork and worry.

The sputum was positive for acid fast bacilli on admission, and the chest roentgenogram taken at that time is reproduced. His temperature was elevated to 100-101 degrees and did not decrease on bed rest. Collapse therapy was deemed inadvisable. One gram of streptomycin was given daily for six weeks with resultant fall of temperature to normal, marked weight gain, decrease in sputum production, and slight clearing of the bilateral pulmonary lesions. The sputum remained positive.

Miscellaneous

Four of our cases could not be placed in any of the above mentioned categories.

D.S., a Filipino, had bilateral hematogenous lesions throughout both lung fields and a stag-horn calculus in one kidney. The sputum and urine were both positive on culture for M. tuberculosis. Because of these findings plus hectic temperature curve and general debilitation the prognosis was considered hopeless. Following an eight week course of streptomycin therapy consisting of 1.8 grams daily, the sputum converted and



CASE 5

the temperature became normal. Nephrectomy was performed with a subsequent pathologic diagnosis of tuberculosis. Chest roentgenograms showed a moderate degree of clearing during this period.

R.S., a 32 year old Negro with pleural effusion, developed paresis of both legs and was explored for a suspected spinal cord tumor. A paraspinal abscess was found, and the sub-dural space was inadvertently contaminated with pus during the procedure. Tuberculosis was considered a likely diagnosis and therefore he was given streptomycin in four gram daily doses for five months. Tubercle bacilli were isolated from the pus removed at operation on cultural and guinea pig examination. At the last observation, 13 months after operation, tuberculous meningitis had not developed despite gross contamination of the sub-dural space with tuberculous pus. The pleural effusion cleared during the course of streptomycin therapy, but the paresis was present at the date of writing. (See Rigdon[23]).

P.L., a 19 year old white male, developed pleural effusion during the course of bed rest treatment for an asymptomatic minimal infiltrate

discovered on a routine chest roentgenogram. The effusion was accompanied by fever to 102 degrees, severe chest pain and dyspnea. Since an acute exudative sub-pleural process was suspected, one gram of streptomycin was given daily for six weeks. The fever disappeared by lysis and the effusion, which was positive on culture for M. tuberculosis, resorbed within six weeks. His sputum remains negative on culture, he continues asymptomatic, and is a quiescent case.

F.T., a 32 year old white male, was hospitalized for six months for an asymptomatic minimal infiltrate discovered on routine chest roentgenogram. During this period the gastric contents were consistently negative on culture. He became acutely ill one evening with chills, prostration, and fever to 102 degrees. The chest roentgenograms revealed multiple fluid levels in a large bulla noted on all films taken previously. The amount of sputum increased markedly and was positive on smear and culture. Streptomycin was given for five weeks in 1.0 gram daily doses. The cystic areas obliterated and the temperature became normal. The sputum remained positive and planigrams revealed what was considered an area of tuberculous cavitation within the once emphysematous area. Therefore thoracoplasty was done.

We consider this a tuberculous infection in a cystic area of lung tissue similar to the pyogenic infections described by Maier and Haight.[24] A detailed report of this case will be made in a subsequent communication.

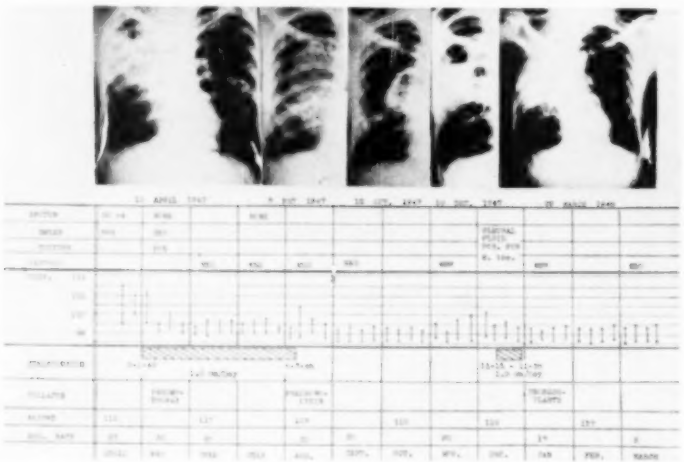
Tuberculous Empyema

Streptomycin therapy has been used in five cases of tuberculous empyema. In three of them, the empyema complicated artificial pneumothorax therapy. In two instances the pneumothorax space was obliterated and the empyema was controlled by thoracoplasty done prior to complete re-expansion of the lung. The third patient refused operation, and the space was obliterated by re-expansion of the lung. One empyema followed lobectomy for bronchiectasis of the right middle lobe which proved tuberculous on microscopic examination. This case died about one year after the empyema developed following extrapleural pneumonectomy. The fifth case presented itself as an empyema necessitatis which apparently followed spontaneous broncho-pleural fistula of tuberculous origin. Streptomycin therapy was used to control the acute initial phase of the disease, and subsequently the destroyed lung was removed along with the parietal pleura and the empyema pocket. (See Sarot and Gilbert[25]). This group is summarized in Table 2, and is exemplified by Case 6.

J.D., a 22 year old Negro, was admitted to the hospital because of chills, fever, and cough productive of about 50 cc. of purulent sputum daily. These symptoms had been present for about two weeks, and during this time there was a 25 pound weight loss.

The sputum was positive on smear for acid fast bacilli, the temperature ranged from 102 to 103 degrees, and the chest roentgenogram is reproduced. He was given 1.8 grams of streptomycin daily for two months and 1.2 grams daily for an additional month. Artificial pneumothorax was

induced at the time streptomycin therapy was instituted, and subsequently pneumonolysis was done. The sputum became negative, but purulent pleural fluid appeared which was accompanied by fever. This fluid was subsequently positive on culture for M. tuberculosis. Streptomycin was given in 1.0 gram daily doses for two weeks with resultant decrease in the temperature to normal, but the fluid remained purulent. The base of the lung was allowed to re-expand during this time, and thoracoplasty was done in one stage to obliterate the space. The empyema was controlled. The remainder of the hospital course was uneventful, and the patient was transferred to a Veterans Administration Hospital for rehabilitation.



CASE 6

Discussion

In gross and microscopic examination of necropsied cases of pulmonary tuberculosis treated with streptomycin Auerbach and Stemmerman[23] observed four effects of the drug. There was a marked decrease in the amount of perifocal reaction about areas of caseation, a great decrease in the incidence of intestional tuberculosis, and of laryngeal tuberculosis, and an increase in the amount of productive reaction at the periphery of caseous and pneumonic areas. These observations help explain many of the effects noted clinically in streptomycin-treated cases.

In correlating the observed effects of streptomycin therapy as noted on chest roentgenograms with the known pathological changes, the most striking effect noted in our series was the rapid clearing of "soft" exudative spreads. This is probably due to dissolution of the perifocal reaction about areas of caseous lobular pneumonia. It is problematical how much of the healing changes

subsequently noted in the tuberculous foci (as judged by the subsequent course of the disease) is due to streptomycin therapy per se, but certainly the elimination of the surrounding perifocal reaction promotes the productive reaction which is important in the healing of tuberculous foci.

The favorable response of confluent tuberculous lobular pneumonia (tuberculosis pneumonia) was particularly striking in this series, and is due to both the clearing of the perifocal reaction and to the stimulation of the production of collagen by the invading productive elements. It is felt that these two factors are of great importance in aborting the extension of the caseation necrosis with its subsequent liquefaction and massive excavation which so often follow in natural sequence in untreated cases.

Acinous nodose foci, which by roentgenogram appear as the nodular type of transbronchial dissemination, do not show so dramatic a decrease in size as do the "softer" areas of caseous lobular pneumonia. This is probably due to the paucity of perifocal reaction which surrounds these lesions in their natural state. Nevertheless, acinous nodose foci have shown more rapid healing after streptomycin therapy than was expected otherwise. Auerbach and Stemmerman have demonstrated that this is due to an increase in the productive elements and also to failure of the centers of these lesions to caseate as extensively as was expected.

There has been considerable discussion regarding the ability of streptomycin to close cavities. In a summary of the results obtained in 223 cases of pulmonary tuberculosis treated with streptomycin by the Army, Navy, and Veterans Administration, Barnwell, Bunn and Walker[9] state that ". . . .of 182 cavities present at the beginning of treatment, 47 (26 per cent) were closed or *lost to view* (italics our own) at the end of treatment . . . ." Cavity closure undoubtedly occurs in certain cases treated with streptomycin. It also occurred prior to the advent of streptomycin therapy, without collapse measures, and without bed rest. We believe that many of the cavity closures observed following streptomycin therapy are more apparent than real; the cavities are "lost to view".

A cavity is visualized roentgenographically because the components of the cavity wall, surrounded by a zone of perifocal reaction, produce an annular shadow on the roentgenogram which contrasts with the remainder of the lung fields. The effect of streptomycin on the relatively evanescent perifocal reaction will produce a rapid resolution which will increase the difficulty in visualizing the cavity. The validity of this hypothesis is supported by the statement of Barnwell et al that "The jurors were impressed by observing thinning of cavity walls . . . .".

Accordingly, we believe in general, that if indications for collapse therapy exist prior to streptomycin administration, they remain following the course of treatment in spite of presumptive evidence from examination of pathologic material is suggestive that the above conclusions are sound.

The healing and/or prevention of laryngeal and intestinal disease undoubtedly accounts for a great deal of the increase in feeling of well-being, improvement in appetite with subsequent weight gain, and decrease of fever noted in these cases. Diminution of the amount of perifocal reaction as a result of streptomycin therapy early in the course of an exudative phase should manifest itself by increased tendency to localization and subsequent healing of a pneumonic or caseous process. Since our cases cannot be contrasted with a control group, the above statements cannot be proved statistically. We believe, however, that the evidence from examination of pathological material is suggestive that the above conclusions are sound.

It should be emphasized that an open cavity discharging viable tubercle bacilli is quite as likely to give rise to a bronchogenic spread during streptomycin therapy as in its absence. We have seen cases sustain an intracanalicular spread with rapid onset of fever, cough, and confirmatory roentgenographic findings while receiving streptomycin therapy. When the effect of streptomycin manifested itself against the organisms in the pneumonic areas, these patients became afebrile, asymptomatic, and their chest roentgenograms cleared. Only if a drug could actually kill or greatly damage most of the organisms being discharged from a cavity could that drug be expected to prevent bronchogenic spreads. This has been shown clinically by the Veterans Administration in a study in which alternate cases of thoracoplasty were given streptomycin therapy during the period of operative treatment. The incidence of spreads was not significently different in the two groups. Thus we have not advised the use of streptomycin to prevent intracanalicular spreads. We believe it is wiser to withhold the drug and if a spread occurs, the organisms will be sensitive and streptomycin can then be used to prevent advantage.

We agree with Muschenheim et al[5] that the regularity with which improvement occurs during and following streptomycin therapy is strong evidence that the drug is beneficial in pulmonary tuberculosis. We believe that Charts 1 to 8 furnish objective evidence that a decrease in the sedimentation rate, sputum production, and daily fever occurred during and following a course of streptomycin treatment.

There is a definite possibility that if streptomycin were given earlier than we have advocated, the use of the drug would not

be necessary in the future course of the disease. By giving it earlier and with less rigid indications, a significantly greater number of cases might not progress to the point where they would need streptomycin according to our indications.

For example, streptomycin therapy is not advocated at this time for tuberculous pleural effusions because most observers would rather save the drug for future use in case progress of the disease might require streptomycin much more urgently than the average pleural effusion. On the other hand, we wonder if earlier antibiotic therapy might not prevent the development of the phthisis which so often follows the effusion even with adequate sanatorium care. If this were so, and if our indications were broadened, a large percentage of all cases of tuberculosis would be candidates for the drug.

The effect of streptomycin therapy on our cases has been evaluated by a "jury" of tuberculosis specialists. A much more satisfactory and reliable method would have been to compare this group with a similar control group. This has been done in England as reported by Hart,[27] and in this country a series of cases with comparable controls has been reported by Jenkins et al[28]. The National Institute of Health is sponsoring a similar but much larger controlled program. The results reported by Jenkins and by Hart reveal definitely better results in the streptomycin-treated group than in the controls.

We believe our series of cases and information in the literature furnish evidence that streptomycin is of definite benefit in certain selected cases of pulmonary tuberculosis. This is so, not because the drug alone can cause any great percentage of cases to become arrested, but because in conjunction with a modern sanatorium regimen and integrated with a program of collapse therapy it can improve the prognosis in a significant number of cases.

There has existed a definite need for an agent capable of effectively treating the acute phases of pulmonary tuberculosis. Although streptomycin is far from being an ideal drug to fulfill this therapeutic need, it is of definite value in selected cases.

SUMMARY AND CONCLUSIONS

1) Seventy-six cases of pulmonary tuberculosis who received streptomycin therapy have been reviewed.

2) Most of them received one gram daily for six weeks following an observation period of six weeks or more during which time the disease progressed, failed to improve, or improved less than was desired or expected.

3) The results obtained were subjected to analysis by a group of specialists who found that 71 per cent of the cases showed

roentgenologic improvement following streptomycin therapy, 83 per cent showed definite over-all clinical improvement, and 59 per cent showed roentgenologic and over-all clinical improvement greater than could be expected without streptomycin.

4) The results for the group are as follows:

Apparently arrested	2 (2.6 per cent)
Quiescent	13 (17 per cent)
Still active	57 (74 per cent)
Prepared for definite collapse therapy	40 (52 per cent)
Dead	4 (5 per cent)*

One of the deaths followed pneumonectomy, one followed tuberculous meningitis, and two resulted from steadily progressive pulmonary tuberculosis.

5) The rationale behind our indications for streptomycin therapy has been discussed.

6) An attempt has been made to correlate the findings observed on roentgenograms of the chest with the observations of the pathologist at autopsy following the use of streptomycin therapy, and an attempt has been made to interpret these changes in anatomic terms.

7) The results have been achieved, we believe, by an integrated program of streptomycin and collapse therapy superimposed upon bed rest.

*All of these cases were autopsied. The clinical histories, gross and microscopic findings have been reviewed by Dr. Oscar Auerbach, and the findings are in agreement with the reported morpholigic changes characteristic of streptomycin treated tuberculosis.[26]

The authors wish to express thanks to Dr. Oscar Auerbach and Dr. J. Maxwell Chamberlain whose interest and encouragement made this study possible.

SUMARIO Y CONCLUSIONES

1) Se revisaron setenta y seis casos de tuberculosis pulmonar tratados con estreptomicina.

2) La mayoría de ellos recibieron un gramo diario después de seis semanas de observación o más y se les administró esa dosis por seis semanas.

Después de un periodo de observación previo de seis semanas o mas durante las que no pudo observarse mejoria, mejoraron menos de lo esperado o empeoraron, se instituyó el tratamiento por seis semanas.

3) Los resultados obtenidos fueron sujetados a un análisis por un grupo de especialistas, quienes encontraron que 71 por ciento de los casos observados mostraron mejoría radiológica después de

la estreptomicina; 83 por ciento mostraron mejoría general en todos sentidos desde el punto de vista clínico, mayor que la que podría esperarse sin la estreptomicina.

4) Los resultados del grupo son así:

Aparentemente detenidos	2	(2.6 por ciento)
Inactivos	13	(17 por ciento)
Aún activos	57	(74 por ciento)
Preparados para cierta colapsoterapia	40	(52 por ciento)
Fallecidos	4	(5 por ciento)*

Una de las defunciones fué después de neumonectomía, otra después de meningitis tuberculosa y dos a consecuencia de tuberculosis progresiva.

5) Se ha discutido la base racional respaldando nuestras indicaciones para la estreptomicinoterapia.

6) Se ha intentado correlacionar los hallazgos observados en las radiografías con los hallazgos de autopsia después de la estreptomicina y se ha tratado de interpretar estos cambios en términos anatomopatológicos.

7) Los resultados logrados creemos que se deben a un plan cooperativo de estreptomicina, colapso y reposo en cama.

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*Todos estos casos fueron autopsiados. Las historias clínicas, hallazgos macro y microscópicos fueron revisados por el Dr. Oscar Auerbach y los hallazgos están acordes con los cambios morfológicos característicos de la tuberculosis tratada con estreptomicina.[26]

REFERENCES

1 Hinshaw, H. C., Feldman, W. H. and Pfuetze, K. H.: "Treatment of Tuberculosis with Streptomycin: A Summary of Observations on One Hundred Cases," *J.A.M.A.*, 132:778, 1946.

2 Hinshaw, H. C., Feldman, W. H. and Pfuetze, K. H.: "Streptomycin in the Treatment of Clinical Tuberculosis," *Am. Rev. Tuberc.*, 54:191, 1946.

3 Council of Pharmacy and Chemistry of the American Medical Association (Manuscript prepared by the Office of the Chief Medical Director of the Veterans Administration, the Surgeon General of the Army and the Surgeon General of the Navy): "The Effects of Streptomycin on Tuberculosis in Man," *J.A.M.A.*, 135:634, 1947.

4 "Annual Report of the Committee on Therapy and the Subcommittee on Streptomycin," *J.A.M.A.*, 135:641, 1947.

5 Muschenheim, C., McDermott, W., Hadley, S. B., Hull-Smith, H. and Tracy, A.: "Streptomycin in the Treatment of Tuberculosis in Humans," *Ann. Int. Med.*, 27:769 and 989, 1947.

6 Streptomycin Committee, Veterans Administration: "The Effect of Streptomycin Upon Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, 56: 485, 1947.

7 Canada, R. O.: "Streptomycin Therapy in Progressive Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, 56:508, 1947.

8 Fisher, M. W., Fishburn, G. W. and Wallace, J. B.: "Streptomycin and Bed-rest in the Treatment of Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, 56:534, 1947.

9 Shamaskin, A., Morris, L. C., Des Autels, E. J., Mindlin, J., Zvetina, Jr. R. and Sweany, H. C.: "Streptomycin in the Treatment of Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, 56:540, 1947.

10 Cassidy, W. A. and Dunner, E.: "Pulmonary Tuberculosis Treated with Streptomycin," *Am. Rev. Tuberc.*, 56:552, 1947.
11 Parnall, C. Jr., Brock, B. L. and Moyer, R. E.: "Streptomycin in the Treatment of Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, 56:565, 1947.
12 Allison, S. T. and Nilsson, J. M. N.: "Treatment of Pulmonary Tuberculosis with Streptomycin," *Am. Rev. Tuberc.*, 56:579, 1947.
13 D'Esopo, N. D. and Steinhaus, J. D.: "Streptomycin Therapy," *Am. Rev. Tuberc.*, 56:589, 1947.
14 Pfuetze, K. H. and Ashe, W. A.: "Present Status of Streptomycin in Tuberculosis," *Dis. of Chest*, 14:446, 1948.
15 Riggins, H. M. and Gearhart, R. P.: "Antibiotic and Chemotherapy of Tuberculosis," *Am. Rev. Tuberc.*, 57:35, 1948.
16 Shields, D. O.: "Tuberculous Pneumonia," *Am. Rev. Tuberc.*, 50:122, 1944.
17 Rich, A. R.: "The Pathogenesis of Tuberculosis," *Charles C. Thomas Co.*, 1944.
18 Laird, A. T.: "Tuberculosis in Elderly People," *Journal Lancet*, 64:208, 1944.
19 Medlar, E. M., Spain, D. M. and Holliday, R. W.: "Disregarded Seedbed of the Tubercle Bacillus," *Arch. Int. Med.*, 81:501, 1948.
20 Medlar, E. M.: "Incidence of Tuberculous Pulmonary Cavities in Unexpected Deaths," *Arch. Int. Med.*, 80:403, 1947.
21 Reisner, D.: "Incipiency and Evolution of Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, 57:207, 1948.
22 Howlett, Kirby S. Jr. and O'Connor, J. B.: "Treatment of Tuberculosis with Streptomycin. Response of Certain Subacute and Chronic Types," *Am. Rev. Tuberc.*, 58:139, 1947.
23 Rigdon, R. H.: "Transverse Myelitis Accompanying Tuberculous Meningitis," *Am. Rev. Tuberc.*, 50:332, 1947.
24 Maier, H. C. and Haight, C.: "Large Infected Solitary Cysts Simulating Empyema," *J. Thor. Sur.*, 9:471, 1940.
25 Sarot, I. A. and Gilbert, L.: "Pneumonectomy, Total Pleurectomy and Thoracoplasty for Uncontrolled Pulmonary Tuberculosis with Broncho-pleural Fistula and Mixed Infection Empyema," *Quart. Bull., Sea View Hosp.*, October 1948.
26 Auerbach, O. and Stemmerman, G. N.: "Anatomic Changes in Tuberculosis Following Streptomycin Therapy," *Am. Rev. Tuberc.*, 58:449, 1948.
27 Hart, P. D'A.: "Clinical and Chemotherapeutic Measures in Tuberculosis 44th Annual Meeting," National Tuberculosis Association.
28 Jenkins, D. E., Peck, W. M., Reid, J. J. R. and Willis, H. S.: "Effect of Streptomycin on Early Tuberculous Pulmonary Lesions," *Am. Rev. Tuberc.*, 56:387, 1947.

A Clinical Analysis and Follow-Up Study of Five Hundred and Two Cases of Carcinoma of the Lung*

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Sixteen years have now elapsed since the first total pneumonectomy was performed in the Johns Hopkins Hospital. Previous to that time a diagnosis of pulmonary malignancy was made infrequently and more for academic than practical reasons. Prior to this time no therapeutic measures or methods were available which offered the patient more than palliation. Medicinal and radiation therapy were then, as now, equally ineffective and the disease when so treated was, and is, always fatal.

The surgical treatment of malignant tumors of the lung has been a boon to patients and a lively stimulus to clinicians interested in pulmonary lesions. Because of this increased interest on the part of physicians, the diagnosis of tumors of the lung is made much more frequently than in the past with the result that a greater number of such patients are being referred for operation. In a medical center in which a special interest in this type of surgery has been manifested, what seems a disproportionate increase in the frequency of these cases is apt to occur, but it may probably be true that the incidence of primary pulmonary cancer is on the increase.

It is the purpose of this report to record the clinical analysis, preoperative preparation, operative procedure, immediate and remote postoperative results in a series of 502 consecutive cases of carcinoma of the lung which have been referred for surgical treatment, not accounting for those instances in which the patient was obviously inoperable from the standpoint of the clinical findings.

Clinical Analysis

Etiology: Although the etiologic factors involved in the production of cancer are unknown, there are enough data accumulated to draw some conclusions as to the influence of certain factors to which human beings are exposed. In this and other series of reported cases one fact has been outstanding as probably playing

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a definite role in the production of pulmonary carcinoma, namely, the great majority of patients afflicted with this malady are residents of urban districts. In such districts, from the cradle to the grave, the lungs are constantly exposed to many irritating substances, such as dust, dirt, various fumes, gases and other atmospheric pollutions which have a deleterious effect on the lining cells of the bronchial tree throughout its entire extent. It is a well known fact that miners in various places in the world, and particularly laborers exposed to certain foreign particles in the air, are very prone to develop growths in the lung. It is also fully recognized that individuals who are working in contact with irritating gases, such as chlorine and others, frequently develop epithelial growths in the air passages. Changes in oxygen tension will affect the type of epithelial lining cells, often causing a metaplasia from the cylindrical cell to a flat cell. This morphologic transposition may also be found in the bronchi which are tributaries to areas of infection, such as lung abscess or bronchiectasis. In other words, chronic irritation, regardless of the type, will produce changes in the growth-rate and shape of the cells of the lung which seem to be very sensitive to this pollution of the atmosphere. It will be interesting now that women are smoking, to see if the much higher ratio of the malignancy of the lung in men, is decreased by an increase in the incidence of malignancy in women.

Due to the occupational hazards mentioned above as well as habits, a higher incidence of primary malignant tumors of the lung is to be expected in the male than in the female. Table I shows the distribution according to sex of the patients in this series. It is to be noted that there is a much higher incidence in the male than in the female, a ratio of almost 6 to 1 in favor of the males. The incidence of involvement of the right and left sides is approximately the same.

In regard to the age incidence of primary malignant tumors of

TABLE I

Distribution According to Sex of Cases of Primary Carcinoma of the Lung and Involvement of Right or Left Side.

	Operable Per cent	Inoperable Per cent
Male	86	85
Female	14	14
Right side	53	51
Left side	47	49

the lung, this does not vary to any great extent from the age incidence of malignant growths elsewhere in the body. The majority of the patients were in the fourth to sixth decade. Perhaps patients in the second to fourth decades were more frequently affected than would be the case of other viscera; however, this series of cases, although relatively large, is far too small to warrant an exact statement. Twelve of the cases fall into the sixth decade. The oldest patient in this series to be operated upon was 79 years of age and the youngest 19. Age, in itself, seems to offer no contraindication to operation. Not infrequently an older patient from a physiologic point of view is a far better operative risk than a younger one. In this series the older patients were surprisingly unaffected by the operative procedure, including the patient 79 years of age, and generally had uneventful postoperative convalescences. Pulmonary cancer, however, generally speaking, is a disease of advanced age.

Unfortunately for the lay public, physicians as a whole (because of the lack of therapeutic measures to combat such lesions or to effectively treat them), have been less acutely interested in the possibility of malignant growths of the lung than those of other viscera or organs of the body. It is, therefore, important that not only all physicians, but also the lay public, should become cognizant of their respiratory tracts in order that they may at the earliest moment seek confirmation or dissipation of their apprehensions in regard to signs and symptoms originating in their respiratory organs. It is mandatory that the knowledge of the signs and symptoms originating as a result of malignant tumors of the lung be made known to the public as a whole, just as every woman knows the significance of a tumor of the breast and realizes the importance of immediately consulting a physician concerning such a tumor.

In the analysis of this series of patients herein reported, in regard to the most frequent signs and symptoms occurring in such cases of primary cancer of the lung, only those signs and symptoms were included that could be attributed to the involvement of the lung itself and not to invasion of contiguous structures or distant metastases. In 71 per cent of the patients in this series cough was the chief symptom. In a nation of heavy cigarette smokers, in which the population supplying the majority of patients breathes the polluted atmosphere of cities, cough is almost universal and is due mainly to nonspecific irritation of the respiratory tract. The important point about coughing that should make one suspicious of the presence of an intrabronchial growth is the departure from the normal for any individual. If in an adult "chronic cougher" the type of cough changes to a spasmodic,

productive or nocturnal type, or, again, if a person who has heretofore coughed infrequently suddenly begins to be annoyed by a hacking cough day and night, attention should be focused on the bronchial tree and the presence of a bronchial neoplasm should be suspected. The development of a cough or changes in the character of coughing can portend an extremely serious condition. Until physicians as a whole, as well as the lay public, become more acutely aware of the serious significance of this sign, the opportunity for early and satisfactory treatment of pulmonary neoplasms will be denied to many patients. It is to be noted, again, that the outcome in this condition, unless recourse is had to surgery, is invariably fatal. These symptoms and signs are listed according to the frequency of their occurrence in Table II.

In 63 per cent of our patients hemoptysis was associated with coughing. This varied from streaking of the sputum to the expectoration of large and copious amounts of blood, up to six ounces (180 cc.). In the latter group the accumulation of blood in the mouth was preceded by a "gurgling" in the chest on one side which warned the patient of the impending hemoptysis. In our experience, copious hemoptysis has usually been associated with the adenocarcinoma type of intrabronchial growth. Unless the roentgenograms and sputum examination are indisputably those of tuberculosis or bronchiectasis, hemoptysis must be considered to be due to an intrabronchial growth until this has been ruled out by the many types of examinations at our command. The burden of proof is on the physician, who, in any given case, states that hemoptysis is not due to a tumor of the lung. This is true even though a small number of tubercle bacilli may be present in the sputum. Tuberculosis and cancer may be associated, and were in four cases in our series. Clinical exam-

TABLE II

Signs and Symptoms of Primary Carcinoma of the Lung.

	Per cent
Cough	71
Hemoptysis	63
Pain	50
Loss of weight	39
Hyperpnea	23
Pneumonitis	18
Fever	13
Tightness in chest	3

inations to diagnose an intrabronchial tumor in no way interfere with the treatment of pulmonary tuberculosis; but if a patient bleeding from a tumor of the lung is observed for months in an attempt to prove the case to be tuberculosis, in many instances he will have lost his only opportunity for successful treatment. The discovery that the bleeding was originally from a neoplasm will have come too late.

Although it is uncommon to have pain as a prominent symptom in cancer of other organs, it is third in prominence among the signs and symptoms in patients afflicted with cancer of the lung. Pain arising from an intrabronchial neoplasm must be differentiated from the pain due to direct invasion of contiguous structures. Pain arising from the lung itself is not associated with the respiratory cycle, as is the pain of pleuritis. It is most often described by the patient as a constant dull ache deep in the chest. The frequency with which the actual position of the tumor, as shown by roentgenography, coincided with the location of the level of pain on the chest wall, as indicated by the patient, was surprising. In all probability pain does not arise within the tumor itself but is a result of pressure on the bronchial wall. Persistent pain in the chest, in the absence of inflammatory disease or aspiration of a foreign body, should always lead to careful investigation of the respiratory tract. Pain down the arm or in the chest wall, so characteristically found in the so-called "superior sulcus or Pancoast tumor," is, as a rule, due to direct invasion of the ribs or the brachial plexus or both. This distribution of pain is considered a very unfavorable symptom from the standpoint of operability.

Loss of weight in advanced carcinoma of any organ in the body, particularly the gastro-intestinal tract, is well known and obvious; but not so easily understood. There was a striking loss of weight in 39 per cent of the cases of pulmonary carcinoma. This loss of weight was, of course, due in part to coughing, loss of appetite because of hemoptysis and sputum, worry, etc.; but the rapid gain of 30 to 50 pounds in a few months after total pneumonectomy for the removal of a relatively small growth remains unexplained.

Fifth on the list of signs and symptoms is hyperpnea, occurring in 23 per cent of the patients. These patients complained of a sudden desire to breathe in deeper breaths, not exactly similar to air hunger but approximating this condition. The deep breathing sensation one experiences when breathing carbon dioxide would seem to be similar. This paroxysmal hyperpnea came on suddenly and lasted for a few seconds or a few hours. The mechanism for this respiratory phenomenon is difficult to explain. It may possibly be caused by a plug of mucus occluding a secondary or tertiary

bronchus already partly plugged by an intrabronchial neoplasm, the bronchopulmonary segment of lung, to which the occluded bronchus is a tributary, thus, becoming the site of an obstructive emphysema. Reflex disturbances in the respiratory rate and amplitude are thus set up. With expulsion of the mucus plug the respiratory rate returns to normal. Such unusual changes in the respiratory cycle, even though of short duration, should excite one's curiosity sufficiently to suggest a thorough examination of the bronchial tree.

Eighteen per cent of the patients had suffered from attacks of pneumonitis associated with episodes of fever and all the signs and symptoms characteristic of pneumonia. It was frequently possible to obtain a history of numerous attacks of so-called "pneumonia" in the recent past. The chief characteristic of these attacks was that they occurred at any time of the year, with apparently no tendency toward seasonal incidence, as in the true epidemic pneumonia. Furthermore, physical signs were atypical and in unusual locations as regards the lung itself. Lobar, broncho- or interstitial pneumonia, as a rule, present fairly typical physical signs. This is not the case in pneumonitis due to bronchial obstruction associated with primary carcinoma of the lung. The explanation for these unusual observations is not far to seek when their pathogenesis is considered. When obstruction of a bronchus, whether primary, secondary, tertiary or quaternary occurs as a result of a new growth, alone or in association with a mucus plug, the bronchial tree peripheral to the point of occlusion becomes filled with mucus. Eventually infection of this bronchopulmonary segment occurs and the clinical syndrome of localized pneumonitis is produced. A portion of a lobe of greater or lesser dimensions, the entire lobe or even the entire lung may be involved. If exacerbations of such a pneumonitis are of sufficient frequency, bronchiectasis or even an abscess, will at times supervene. Often such an abscess perforates into the pleura and produces putrefaction empyema. The point to be emphasized is that when such an unusual sequence of events takes place, or when any one of the previously mentioned inflammatory episodes occurs that cannot be explained as a complication of a typical pneumonia or as a result of aspiration of a foreign body, an intrabronchial growth should be suspected. It is the repetitious nature of such pneumonitis which makes it so significant.

In general, it may be stated that there are no characteristic or pathognomonic signs and symptoms of primary carcinoma of the lung. This lesion masquerades many of the more common disorders of the lung. The onset is often insidious, but the recurrent nature of signs and symptoms previously described should call

attention of the patient and the physician to the respiratory tract so that a thorough examination will be carried out. Especially is this true of a patient who has previously had excellent health and in whom, after the second decade, there develops a cough associated with hemoptysis. Too often precious time is lost because of a diagnosis of pulmonary tuberculosis, lung abscess, unresolved pneumonia, bronchiectasis or heart disease. The methods of examination employed to rule out the presence of an intrabronchial growth in no way interfered with the diagnosis or treatment of any of the conditions which are at times mistaken for such a growth.

Diagnosis: In this series of 502 cases the roentgenograms of the chest were positive in every instance. It is not suggested that a diagnosis of primary carcinoma of the lung could be made from the roentgenographic studies alone, but there was in each case an abnormal shadow which necessitated further study and examination. Thus, it may be stated emphatically that in every instance in which roentgenograms of the chest show a departure from normal, and in which this departure is not in every way characteristic of one of the commoner lesions of the lung, the presence of bronchogenic cancer should be inferred. Unquestionably, the roentgenograms of the chest are the most important and simplest method of examination at our disposal. Even in the earliest stages of growth of a primary carcinoma of the lung the lesion, as a rule, can be discovered. In the early part of the last decade, and even today, it was, and is, disheartening to watch an early lesion develop over a period of months into an inoperable cancer of the lung because physicians who were not, and are not, aware of this danger would advise the patients to "wait and see what happens." "Coming events often cast their shadows before them." It is equally true that shadows cast by hilar infiltration due to other conditions, such as tuberculosis and even normal structures, are confusing. However, an infiltrating hilar shadow in a patient past middle age, associated with cough, hemoptysis and the absence of tubercle bacilli in the sputum almost certainly indicates a bronchogenic carcinoma. Most of these carcinomas are located at or near the hilus or root of the lung. The diagnosis of cancer of any organ cannot be definitely made by roentgenologic examination alone, but the more experienced the observer is the greater is the likelihood of an accurate interpretation. Positive roentgenograms may show a shadow caused by the new growth itself or by an area of atelectasis, bronchiectasis, pneumonitis, or abscess caused indirectly by occlusion produced by the growth of a bronchus leading to a bronchopulmonary segment or segments.

In my experience, second to the roentgenogram in importance

in yielding information which is helpful in arriving at a definite diagnosis is bronchoscopy. In fact, either by direct vision or biopsy or both a positive diagnosis of primary carcinoma of the lung can be made only in this manner. In 50 per cent of the patients in this series a positive biopsy of the cancer was obtained. A pulmonary new growth in the periphery or even in the hilar lesions confined to the upper lobes may be beyond the vision of the bronchoscopist. Nevertheless, valuable information can be elicited by bronchoscopy even when the growth cannot be seen, such as fixation or deformity, or both, due to pressure of any visible portion of the bronchial tree. The presence of blood or purulent discharge from certain bronchi serve as a lead. In this series of cases there have been no untoward results during or after bronchoscopic examinations.

Bronchography is a useful diagnostic method only to reveal occlusion of a bronchus by a small growth which does not produce a shadow in the roentgenograms of the chest. It is a harmless procedure and may be the link in the chain of evidence pointing to the possible presence of carcinoma of the lung.

Transthoracic aspiration biopsy has a limited field, is often difficult to interpret, and such procedures are not without danger of implanting some cells along the tract of the aspiration needle or infecting the pleural cavity with the same cells, with tubercle bacilli or other pyogenic organisms. Aspiration of the bronchial tree has in some instances revealed cancer cells which could be obtained for microscopic examination.

Exploratory thoracotomy should be resorted to far more frequently in the future than it has in the past. This is, with the present-day anesthesias and surgical technic, a relatively harmless procedure—far more so than exploratory celiotomy and attended with fewer dangerous sequelae, such as adhesions. Exploratory thoracotomy is far less incapacitating than celiotomy. When it has been impossible to arrive at a definite diagnosis by all the means at our disposal, this procedure should be performed at once, if a dangerous pulmonary lesion such as primary carcinoma is suspected. In our series of cases no deaths have occurred as a result of simple exploration of the chest. If direct observation and palpation of the lesion does not reveal the true nature, excision of the entire area in the lobe should be performed for immediate microscopic examination, and the diagnosis is made as is customary for questionable cases of carcinoma of the breast. If further discussion of the situation with the patient seems advisable, the wound may be closed and the patient returned to his room for further consultation. Later in the week the chest can be reopened and the definite procedure carried out. The old idea that opening

the thoracic cage at operation is another form of euthanasia must be abandoned. The impression that all primary malignant tumors of the lungs are slow-growing and late in metastasizing is incorrect.

Pathology: The surgical removal of primary carcinoma of the lung in a relatively early stage has brought about changes in our ideas of the origin and nature of the growth of such tumors. In the past practically all the data were based on the necropsy in very late cases, when it was impossible on account of the almost universal involvement of the lung and contiguous structures to determine the nature, origin and progress of the growth within the lung. In this series of cases the majority of the tumors occurred at or adjacent to the hilus, the minority in the periphery of the lung. The latter seemed to spread throughout the area of the lung in which they originated by centrifugal growth, most of them apparently having arisen in the alveolar lining cells. The hilar tumors, all of which were bronchogenic in origin, grew grossly in two separate fashions. The one, an intrabronchial tumor arising apparently from the bronchial mucosa, grew into the lumen of the bronchus and towards the trachea. The centripetal tendency of the growth, occluding completely or partly the primary or secondary bronchus was characteristic. The other type of hilar growth was an extrabronchial tumor which, probably arising in the wall of a secondary, tertiary or quaternary bronchus, would break through the wall and grow along outside of, and often completely around the bronchus. This type of growth also showed this centripetal tendency, growing around and about the secondary and primary bronchi and then spreading directly into the mediastinum to involve its structures.

The clinical course is dependent to a great extent on the method of growth. It is obvious that the intrabronchial type will produce respiratory difficulties, cough, sputum, and hemoptysis much earlier than the extrabronchial tumor. The first symptoms caused by the latter method of growth may be, for example, interference with the venous return from the neck owing to the involvement of the superior vena cava on the right side, recurrent laryngeal palsy on the left, or Horner's syndrome. Malignant tumors arising in the periphery are, as a rule, asymptomatic. They may be said to arise in the silent area of the lung and as they do not, as a rule, produce bronchial obstruction or erode pulmonary vessels; the symptoms and signs are usually those dependent on invasion of the pleura and chest wall and, by direct extension, the brachial plexus.

In 70 per cent of the 158 patients upon whom a total pneumonectomy was performed there were metastases to the bronchial and tracheal lymph nodes. This fact emphasized the necessity

of performing a total pneumonectomy with dissection of these regional nodes in order to effect a permanent cure. In the remaining 344 cases that were inoperable, in addition to the metastases in the regional nodes the various organs and structures that were the site of metastases are listed in the order of the frequency of their involvement; namely, supraclavicular and axillary lymph nodes, liver, pleura, pericardium and heart, contralateral lung, osseous tissue, brain and multiple areas in the skin and subcutaneous tissue.

The characteristic histologic structure of the tumor occurring in this series of cases (Table III) was that of a flat and squamous cell carcinoma and adenocarcinoma. Under these two main headings were included various examples such as oat cell, cylindrical cell and adenocarcinoma thought to be different forms of the same tumor. The adenocarcinoma type is pleomorphic. Sections of the tumor differ depending upon the region from which they were cut. Sixty-four per cent of the cases in this series were composed of a flat or squamous cell cancer and 36 per cent the adenocarcinoma group. It is interesting to note the length of life, computed on the basis of the microscopic characteristics of the tumor, showed that those afflicted with the squamous, or flat cell type, lived a greater length of time than those with the adenocarcinoma type.

Treatment: For several days preceding operation the patient should be carefully prepared. It has been our custom to treat the patient with intramuscular injection of penicillin 30,000 units, every three hours, avoiding awakening the patient at night. In addition to this penicillin aerosol should be employed. Whether or not some of the sulfonamides should be used has been questioned. It is my personal opinion that for some days, approximately three, sulfamerazine may be administered by mouth. The

TABLE III
Pathology

	Per cent
Squamous cell carcinoma	50
Flat cell	14
TOTAL	64
Adenocarcinoma	28
Cylindrical cell	4
Oat cell	4
TOTAL	36

patients thus have a protective blood level of this drug which apparently does no harm. It is merely an added questionable merit and so far we have not been able to observe any demerits.

The preoperative preparation which we consider of the greatest importance is the induction of artificial pneumothorax. The advantage of this procedure has been proved over a period of years. In the first place, it must be considered a therapeutic test, particularly in individuals in the fifth or sixth decade in which there may be a certain degree of unrecognized emphysema. Removing the lung at operation without knowing whether or not the patient can sufficiently oxygenate himself with the remaining lung may constitute a fatal error, and in the past we have experienced this tragic result. The ability of the remaining lung to function sufficiently for the needs of the patient can be established before operation is performed by merely collapsing the lung on the affected side. Various tests, such as oxygen saturation of the blood at body rest and during exercise of various degrees of intensity can be ascertained. After all, to cure a patient of a malignant tumor of the lung is futile, if the patient is left with insufficient aeration surface to support normal respiration. There are other minor advantages and secondary ones associated with artificial pneumothorax, such as diminishing the size of the lung so that the mechanical handling of this structure is technically made easier at the time of operation. The patient has learned to breathe with one lung previous to operation and with the increased intrapleural pressure, thus, avoids pleural shock on opening the thoracic cavity. The blood flow through the collapsed lung is less than through the expanded contralateral lung and, therefore, the strain on the right heart from shifting greater blood flow through one pulmonary artery is graduated. The location of a growth as regards the position relative to the mediastinum is often silhouetted and, therefore, ascertained more accurately in the collapsed lung than with an expanded lung.

Operative Intervention: In our present state of knowledge the only efficacious method for treatment of pulmonary carcinoma is by surgical removal of the entire organ, together with the regional lymph nodes. Medicinal and radiation therapy is of no benefit. It is interesting to note that in 344 cases of this series which were found to be inoperable at the time of exploration of the thoracic cavity, the average length of life after leaving the hospital was approximately five months, and this in spite of the fact that every type of supportive therapy, and in many instances, radiation therapy, were employed. It is to be emphasized again that the disease runs a fatal course in 100 per cent of the patients

in whom the lung cannot be removed in its entirety by operation. From an anatomic standpoint, the lung lends itself to surgical removal more readily than any other organ in the body, with the possible exception of the breast. From the point of view of the biologic characteristics of primary carcinoma of the lung, surgical removal is more apt to be successful because of the relatively slow growth and spread of these tumors as compared to similar tumors in other regions of the body. Finally, the remarkable ability and tendency of the contralateral lung to undergo compensatory changes prevents incapacitation of the patient.

Operative Technic

The operative technic now employed for one-stage total pneumonectomy in the treatment of malignant tumors is essentially the same, except for closure of the bronchus, as that described by the author in 1933 in the Johns Hopkins Hospital Bulletin.[1]

A number of points in the operative technic, as would be expected, are still controversial and as in any other operative procedure an unanimity of opinion as regards the various methods is hardly to be expected. But, after 16 years' experience and having employed this operative technic in 502 cases of which 158 were total pneumonectomies, it is felt desirable, with the background of this experience to discuss certain steps in the operative procedure which are of special interest.

In the first place, the anterior approach is definitely to be preferred to the posterior or lateral for the following reasons: (a) the width of the intercostal spaces is greater anteriorly than posteriorly and the necessity for resection of ribs is, therefore, as a general rule, not necessary. This reduces the operative time and the general ill effects of the procedure upon the patients. The thoracic cavity is more quickly entered with a minimum amount of damage to the chest wall and parieties. The use of a self-retaining retractor gives sufficient exposure so that the question of operability can be promptly judged. The time consumed from the incision to the entrance of the pleural cavity is far less when the anterior approach is employed, and associated with this there is a minimum loss of blood as well as trauma to tissues. If a greater amount of exposure is desired the adjacent intercostal cartilages can be incised and the ribs, usually the third and fourth, can be displaced cephalward or caudalward. Also, by slightly rotating the patient on the operating table, or the table itself, if desired, the incision can be extended laterally so that the maximum exposure can be obtained. If the tumor proves to be inoperable, the minimum of operative trauma has been incurred. The operability can be determined at once with the minimum operative

effort. In the event the growth is operable, the dissection of the hilar structures, such as the pulmonary artery and veins which lie anterior to the bronchus, is accomplished with far greater ease and facility when the anterior approach is employed. The advantage of ligating the pulmonary artery at the beginning of the operation is obvious, the control of hemorrhage is, thus, more certainly assured and the greater percentage of blood normally contained within the lung is returned to the general circulation via the pulmonary veins. Bleeding from any adhesions that may exist between the visceral and parietal pleura is reduced to a minimum.

If for any reason it is felt desirable to interrupt the operative procedure and perform the operation in two stages, one can do so after ligation of the pulmonary artery, provided the pulmonary veins have been left intact. If the latter are ligated, the lobe which either one or both pulmonary veins drain, must be removed, for otherwise, gangrene of this portion of the lung will ensue. It is to be noted that the bronchial veins are vestigial in character and do not function sufficiently to even drain off the blood brought to the lung by the bronchial artery, to say nothing of that from the much larger pulmonary artery. When the pulmonary artery, which carries venous blood is ligated collateral circulation through the bronchial artery is at once established. The bronchial artery brings sufficient arterial blood to the lung to maintain this organ in a normal state of nutrition and the circulation through the lung is, thus, changed from a venous to an arterial one. Whereas normally the greater amount of blood flowing through the lung capillaries is venous in character, originating from the pulmonary artery, the blood flowing into the same capillary bed from the bronchial artery is arterial. Stoppage of the blood flow from the pulmonary artery by ligature of the latter, incurs a great increase in flow from the bronchial artery and, thus, fills the capillary bed in the lung and the branches of the pulmonary artery up to the point of ligation with arterial blood, containing such a high saturation of oxygen that the lung is, thus, rendered essentially functionless as far as further oxygenation of the blood flowing through it is concerned. The development of this collateral circulation via the bronchial artery invariably results after ligation of one or both pulmonary veins in moist gangrene of the corresponding lobe or lobes because of the vestigial character of the bronchial veins. In the event of ligation of a pulmonary vein that portion of the lung whose venous bed is a tributary to that vein must be removed at the time of operation.

Not infrequently total pneumonectomy may be carried out with

a greater degree of safety if a two-stage operation is performed, in which only the pulmonary artery is ligated as the principal objective of the first stage. This is particularly true when the lung is the site of a great deal of infection and extensively adherent. The arterialization of the lung with a flow of more highly oxygenated blood would appear to have a beneficial effect on the pulmonary infection and, therefore, the patients' clinical condition.* Dividing the operation into two stages greatly diminishes the shock of the procedure. It has been found that the pulmonary vessels, the artery and veins, are best ligated with silk, or cotton, and in no instance has this type of ligature been known to cut through the vessel wall.

Treatment of the Bronchial Stump

Since 1942, when the method of closing of the bronchus was first reported by the author in the "Annals of Surgery"[2] the bronchial stump has been occluded by the use of mattress sutures of interrupted silk or cotton placed through the bronchus in such a manner that the posterior membranous portion is approximated to the anterior cartilaginous wall, somewhat proximal to the end of the amputated stump, thus creating a viable cuff from 1 to 2 cm. distal to the suture line which immediately fills with a fibrinous clot that thereafter becomes infiltrated with cells and eventually forms a fibrous plug. One of the more important steps in securing a satisfactory closure of the bronchial stump is to sew a pedicle flap of parietal pleura over the end of the stump of the bronchus approximating the pleura to the rim of the viable cuff. The use of any form of cauterization or traumatization to the end of the bronchial stump has been studiously avoided in order that agglutination of the rim of this cuff and the pleural membrane would be brought about immediately and permanently. Any foreign material such as sutures in the end of this cuff or devitalization of the rim of this cuff will militate against the

*In patients suffering from pulmonary tuberculosis ligation of the pulmonary artery has a definite deleterious effect. In eight patients the pulmonary artery was occluded with the idea of bringing about an atelectasis of the lung. The lesions were very extensive in each case and associated with large cavities. However, the change from a lower oxygen tension in the blood flow through the lung following ligation of the pulmonary artery, to the higher oxygen content of the blood flow from the bronchial artery exercised a most marked detrimental clinical and pathological effect on the patient and lung. This was apparent by a more rapid progression of the manifestation of the disease than would have been expected had the pulmonary circulation not been interfered with at all. No atelectasis was produced and cavitation increased rapidly. This unfavorable result was attributed to the fact that the tubercle bacillus flourished in an environment of higher oxygen content. It would be interesting to find out the effect of ligation of only the bronchial artery in pulmonary tuberculosis. The reverse condition of oxygen saturation would then obtain.

immediate healing. Therefore, the bronchial stump should be sutured at least a centimeter proximal, if possible, to the point at which amputation is anticipated. Regardless of the type of suture material or the manner in which it is placed, cutting through the posterior or anterior membranous portion of the bronchus will frequently occur. This has been proved experimentally and at necropsy.[2] Unless every opportunity is, therefore, afforded for the bronchial cuff distal to the suture line to heal by the formation of granulation tissue within its walls leakage will follow in a rather high percentage of cases. In the event that the bronchial growth extends up toward the carina, the bronchus and also the lower end of the trachea may be sutured after a diagonal incision in this structure has been made. This suture, as in the bronchus, should be tied sufficiently tight to approximate the walls of the bronchus or trachea, but not enough to cause crushing of the tissue. If so, the sutures will cut. They should also be placed so that the knots are tied about the cartilaginous rings, that is, on the anterior surface of the bronchus or trachea. Healing of the stump takes place at the cut end and the sutures which occlude the lumen of the bronchus, usually from four to six in number, must be considered as only temporary, with their main purpose to exclude the passage of air through the bronchial stump long enough for the healing of the end of the bronchus to be completed, or sufficiently so, that in the event the sutures cut through, to form a tight and impenetrable occlusion of the bronchial stump that will not open up and allow air to pour into the pleural cavity. The healing of the end of the bronchial stump requires, as a rule, from one to two weeks, varying in different individuals and seems to be completed in the majority of cases after a period of 10 to 14 days. However, there have been instances in our series in which the stump in one patient reopened after a month, one after three months and one even after eight months. However, these, fortunately, eventually healed, but only after thoracoplasty was performed.

Interrupted mattress sutures may be employed by stitching the anterior cartilaginous wall laterally, infolding the posterior membranous portion, providing the cartilaginous rings are incised at the apex of their arc, this in the midline of the anterior surface of the bronchus. This method has been satisfactorily employed in some cases. All types of suture material have been used—catgut, silver wire, steel wire, fascia, and others—and it is our opinion that interrupted sutures of silk or cotton would seem to be the material of choice.

Before the bronchial stump is sutured, after amputation of the lung, the inside of the remaining bronchus should be carefully

inspected, for not infrequently a blood clot or even a piece of tumor tissue may be dislodged from the lung into the primary bronchus during the course of the operation. Immediately following operation the patient is again bronchoscoped while on the operating table before being returned to the ward. Often small clots and pieces of tumor tissue have been discovered not only in the bronchial stump on the operative side but even in the trachea. If these foreign bodies were not removed, aspiration into the contralateral lung might eventuate in the death of the patient.

Mobilization of the parietal pleura may be accomplished on either side by loosening the pleura from the endothoracic fascia either anteriorly or posteriorly in the vertebral gutter. No difficulty has been experienced in obtaining a sufficient amount of pleura to cover over completely and without tension the entire raw hilar area.

At the end of the operation 150,000 units of penicillin and 1 gram of streptomycin have been introduced into the thoracic cavity. The intrapulmonary pressure, as the wound in the chest wall is closed, has been increased to not more than 10 mm. of mercury. The entrapped air is removed to the fullest extent possible by leaving a small catheter in the wound during closure. After the last interrupted suture is placed in the skin all the air that can be is removed by aspiration and the catheter itself is then withdrawn. No drainage of the pleural cavity is thought desirable even in the presence of infection, within the lung itself, and when purulent material has been unfortunately and accidentally spilled into the pleural cavity.

Since penicillin and streptomycin have been available, when gross infection has been present, it has been our custom to introduce every other day 150,000 units of penicillin and 1 gram of streptomycin into the thoracic cavity. In addition, the drugs are also given intramuscularly. No instances of empyema have been encountered in cases so treated, and, thus, the necessity for performing thoracoplasties to obliterate infected dead space in the thoracic cavity has been avoided, except in those instances mentioned above in which bronchial fistulae developed from one to eight months after operation.

A word of caution should be given here in regard to the possibility of the development of interstitial pulmonary emphysema as a result of increasing the intrapulmonary pressure either too rapidly or to too great an extent, in an endeavor to hyperdistend the lung on the unoperated side for the purpose of obliterating the dead space in the thoracic cavity on the operative side. Rupture of aveoli within the lung substance itself producing a mediastinal, plus extensive subcutaneous as well as visceral em-

physema was encountered in one case of diaphragmatic hernia followed by death from cerebral and coronary air emboli, proved at necropsy.

The final proof of the efficacy of any method of therapy naturally is a critical analysis of the immediate and remote results. Of 502 cases of primary carcinoma of the lung, as shown in Table IV, 344 or 69 per cent, were inoperable, whereas 158, or 31 per cent were operable. This ratio of the inoperable to the operable cases is far higher than it should be, for in the majority of instances the attending physician and even the patients had been aware of a lesion in the lung for many months, and often years, before submitting themselves to operation. Undoubtedly in the future, as the field of thoracic surgery is developed, this disproportion will be reduced. There will always be those instances in which a malignant tumor begins in the periphery of the lung, the so-called silent area, and produces no symptoms or signs until involvement of the pleural or contiguous structures renders the case inoperable. Fortunately, this group comprises only about 10 per cent of the cases of malignancy of the lung, 90 per cent occurring near the hilus, and producing warning signals early in the process of the disease. Unless for palliative reason, to rid the patient of an infected lung due to neoplastic bronchial obstruction, for example, pneumonectomy should not be performed if the tumor has involved contiguous structures. Therefore, inoper-

TABLE IV

Total number of pneumonectomies			225
	Per cent		
Number living	102 - 45		
Number deceased	123 - 55		
	225 - 100		
Carcinomas:		Per cent	
34 per cent living	54		
66 per cent deceased	104	158 - 70	
Inflammatory:			
71 per cent living	48		
29 per cent deceased	19	67 - 30	
		225 - 100	
			Per cent
Total number of pneumonectomies for operable carcinoma		158	- 31
Total number of inoperable carcinoma of the lung		344	- 69
		502	- 100

ability would be manifest by involvement of the parietal pleura or any of the underlying structures.

The clinical findings, which we have found to indicate a spread of the tumor beyond the confines of the lung and, therefore, render the case incurable from a surgical standpoint, are the following: Metastases to the opposite lung or mediastinum, direct metastases to brain, osseous tissue, liver, skin, axillary and supraclavicular nodes, pleural effusion, clear or serosanguineous, continuous pain to shoulder or referred down the arm. Horner's syndrome, left recurrent laryngeal palsy or hemiparalysis of the diaphragm.

All patients with lesions of the lung which have been diagnosed probable malignant tumors should be explored regardless of the size or position of the tumor or the age of the patient. In the absence of clinical signs or symptoms of a spread of the disease from within the limits of the lung itself, the question of operability can be determined only by exploration of the chest.

TABLE V

Pneumonectomy for Carcinoma of the Lung
Operations and Mortality According to Years

	No. of Operations	No. of deaths	
1933	2	0	
1934	1	1	
1935	5	2	
1936	5	3	
1937	5	0	
1938	7	2	
1939	6	2	
1940	10	0	
1941	13	4	
1942	10	5	
1943	8	2	
1944	12	3	
1945	15	6	
1946	12	1	
1947	20	4	
1948	21	5	
1949	6	1	
	158	41	26 per cent

In this series of cases, there have been 158 in which total pneumonectomy was performed for carcinoma of the lung. All deaths within one month following operation were considered in the group of immediate postoperative mortality because of the fact that the patients had remained in the hospital that long, although in some instances death was in no way connected with the actual operative procedure. From 1933 through 1939 there were 31 cases with ten deaths, or a mortality of 32.2 per cent. From 1940 through 1946, 80 patients were operated upon, with

TABLE VI

Total Pneumonectomy
Showing Comparison Carcinomas with Inflammatory

	NUMBER OF CASES					
	Carcinoma	Per cent	Inflamm.	Per cent	Total	Per cent
Patients dying after various periods of time:						
Less than 1 month	41	26	13	19	54	24
1 month to 6 years:						
1 month to 6 years	25		4			
6 months to 1 year	19		1			
1 year or more	11		0			
2 years or more	3		1			
3 years or more	3		0			
5 years or more	1		0			
6 years or more	1	40	0	10	69	30
	104	66	19	29	123	54
Patients living:						
Less than 1 month	1		1			
1 to 6 months	3		2			
6 months to 1 year	5		6			
1 year or more	13		4			
2 years or more	9		7			
3 years or more	3		10			
4 years or more	4		4			
5 years or more	3		5			
6 years or more	3		2			
7 years or more	2		2			
8 years or more	3		2			
9 years or more	0		1			
10 years or more	0		1			
12 years or more	3		1			
14 years or more	1		1			
16 years or more	1		0			
	54	34	48	71	102	46
					225	100

21 deaths, or a 26.2 per cent mortality. Thus, in spite of an increase in the number of patients there was a 6 per cent decrease in immediate postoperative mortality. In the last 59 cases there were eleven deaths or a mortality rate of 18.6 per cent. Undoubtedly in the future this hospital death rate will be decreased because of several reasons, such as earlier reference of cases by the general practitioners, improvements in operative technic, chemotherapy and anesthesia. In addition, postoperative care has improved remarkably. Penicillin is now given intramuscularly, by inhalations, and intrathoracically, so that the chance of developing a postoperative empyema is almost nil.

Important as the immediate operative mortality is, and it should be very jealously guarded, the efficacy of the operative procedure should also be judged by the ultimate results. The duration of life following total pneumonectomy for carcinoma of the lung is shown in Table VI. It is to be noted that patients dying after various periods of time are so charted in comparison to patients still living following operation. Those dying following operation who died less than one month afterwards were considered an operative mortality. The total operative mortality of the 158 cases for total pneumonectomy for carcinoma of the lung was 26 per cent. Of the patients who are now dead, but who lived for various periods of time after operation, i.e., from one month to six years, the number surviving the different periods of time was 63. This group of cases made up 40 per cent of the total. Reference must be made to the fact that of the 344 cases of inoperable carcinoma comprising this series, the average duration of life after exploration of the thoracic cavity was five months, so that even in the group in Table V, which are now dead but lived various periods of time following operation, the average duration of life after removing the lung was greater by far than in those patients in which the lung could not be removed. Of the patients living at the present time, 34 per cent of the total, or 54 patients, have survived from one month to 16 years. Of this group, 15 patients have lived five years or more: one 16 years; one 14 years; three 8 years; two 7 years; and three 6 years. As they are still living there is a possibility they may live for many years. It would seem desirable to call attention to the fact that all of these patients, except one who was a professional boxer, have been restored to their normal activities. They have been able to return to their former vocations and even recreations, such as golf, swimming, fishing and hunting. In all except the occasional case, since it has not been found necessary to perform a thoracoplasty, no deformity of the patient is visible from the removal of the affected organ. The remaining lung expands to fill the dead

space. This intrathoracic readjustment has been reported in detail elsewhere. If these results are compared to those obtained from the surgical treatment of carcinoma of the thyroid, breast, esophagus, stomach and large and small intestine, reported over a corresponding length of time (16 years) it will be evident that removal of the lung for primary carcinoma offers at least as great if not greater probability of permanent cure as the surgical treatment of carcinoma of any other organ in the body.

Of the group of patients who lived for some time (up to six years) following operation, but who are now dead, the majority were definitely improved by relieving the coughing, hemoptysis and often extensive pulmonary suppuration with its attendant discomfort and manifestations.

SUMMARY

An otherwise fatal disease, primary carcinoma of the lung, can be satisfactorily treated by surgical removal of the entire organ. Surgical measures short of total pneumonectomy are not efficacious. Postoperative mortality and longevity are at least as good as, if not better than, the postoperative results following the surgical treatment of carcinoma of other organs.

RESUMEN

El carcinoma primitivo del pulmón, enfermedad que de otra manera es fatal, puede ser tratado satisfactoriamente mediante la extirpación quirúrgica del órgano entero. Con la excepción de la neumonectomía total, ninguna medida quirúrgica es eficaz. La mortalidad y longevidad postoperatorias son por lo menos tan buenas, si no mejores, que los resultados postoperatorios que siguen al tratamiento quirúrgico del carcinoma de otros órganos.

REFERENCES

1 Rienhoff, William F. Jr.: "Pneumonectomy: A Preliminary Report of the Operative Technic in Two Successful Cases," *Bull. Johns Hopkins Hosp.*, 53:390, 1933.

2 Rienhoff, William F. Jr., Gannon, James Jr. and Sherman, Irwin: "Closure of the Bronchus Following Total Pneumonectomy: Experimental and Clinical Observations," *Ann. Surg.*, 116:481, 1942.

Discussion

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We have gone a long way in our therapeutic approach to the problem of pulmonary carcinoma. The question of an early diagnosis is still an important one. This situation is partly due to the

fact that the patient often disregards for a long time, a cough, chest pains and other symptoms when valuable time is lost. The physician may also lose valuable time.

Cancer of the bronchus does not show directly on the x-ray until it is in a very advanced stage. Nevertheless the fact that it causes more or less pronounced stenosis makes possible its rather early detection.

While on the Reception Service of the Veterans Administration Hospital at Legion, Texas, we admitted for a period of 18 months 482 veterans of World War I and several of the Spanish-American War. Among this group of mostly middle aged men we found 15 cases or 3.1 per cent to have pulmonary carcinoma. All of these were previously diagnosed and treated for pulmonary tuberculosis and were sent to us for continuation of this treatment. Only one of these patients had an occasional positive sputum and was found to have pulmonary carcinoma with tuberculosis. Three had metastatic lesions in the lungs, 11 had bronchogenic carcinoma. Only one of these patients was operable. There was a time in each one of these patients' lives when he could have been helped.

Intrathoracic Pheochromocytoma
Report of a Case

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Whereas neurogenic tumors of the mediastinum are frequently encountered and removed by thoracic surgeons, the occurrence of the dangerous pheochromocytoma is truly rare. According to the review of intrathoracic tumors of the sympathetic nervous system by Hollingsworth,[1] only two such cases had been reported up until 1946. More recently, Cahill[2] has stated that three pheochromocytomas have been found in the thorax; one of these was reported to him in a personal communication by Mayer. A fourth such case, presented herein, is featured by:

1) Its failure to produce significant symptoms or hypertension preoperatively.
2) A violent hypertension followed by a dangerous fall in blood pressure during the operative removal.

CASE REPORT

O.P. — R.H.O. No. 5856, June 1948: This 16-year-old Peruvian male was seen in consultation in regard to an asymptomatic tumor in his left hemithorax first revealed in January 1948, as a result of a routine chest roentgen-ray inspection. No pulmonary symptom could be elicited. It was brought out in the general interrogation that there was a definite history of mild heat intolerance. The patient was accustomed to strenuous physical exercise and prided himself on his physical prowess. The past illnesses and the family history were non-contributory.

Physical examination revealed the patient to be extremely well developed and muscular. The pulse was 72 per minute and regular in rhythm. The heart was normal in size, shape and sounds. There were no murmurs. The blood pressure was 110/75. The remaining examination, including a neurological examination, was negative. There was no tenderness on percussion over the vertebral spines.

Roentgen-ray inspection of the chest (Fig. 1), with AP and lateral projections, showed an area of density in the left thoracic gutter measuring approximately 3.5 cm. in diameter and 6.5 cm. in length. This abnormal area was homogeneous, and the contour almost smooth. There was no evident involvement of the adjacent bones or of the lungs. The latter appeared clear. Cardiac and diaphragmatic shadows appeared normal.

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Impression: Posterior mediastinal tumor, probably of neurogenic origin.

A clinical diagnosis of posterior mediastinal neurofibroma was made, and the patient was admitted to the New England Deaconess Hospital where his preoperative systolic blood pressure on two occasions was 100 and 120 mm. Hg. Urinalysis and hematologic studies were normal. The fasting blood sugar was 105 mgm. per cent and the N.P.N. was 41 on two occasions.

Operation

On June 30, 1948, left thoracotomy was performed. Anesthesia consisted of cocainization of the pharynx, larynx and tracheobronchial tree for the intratracheal intubation, posterior intercostal block and incisional infiltration with ½ per cent procaine containing six minims of epinephrine 1:1000 solution and cyclopropane, ether and oxygen by inhalation.

Behavior of the Blood Pressure: When the patient was placed on the operating table, the blood pressure was found to be 240/160 mm. Hg., and the pulse was 160 per minute. Shortly thereafter, the blood pressure rose to 270 mm. Hg. systolic. This marked hypertension immediately created the suspicion that the lesion was an epinephrine-secreting tumor

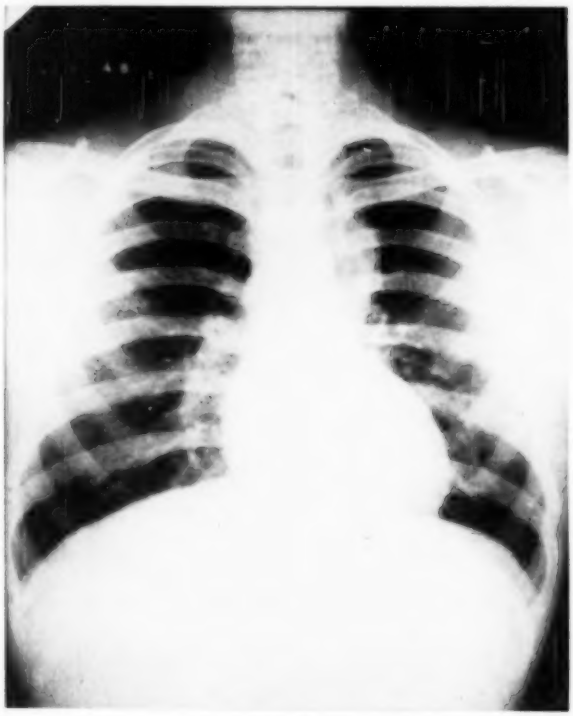

FIGURE 1

of the chromaffin series. It was decided to proceed with the operation. It was considered likely that when the vascular supply to the tumor had been divided, there might be a precipitous fall in blood pressure and, therefore, four pints of blood were held in readiness. Before the incision was made, the blood pressure was 230 mm. Hg. It continued down to 170 as the incision was commenced, but rose again to 230 as the muscular layers were divided. The amount of bleeding was much greater than usual. The blood pressure remained over 180 systolic until all the vascular supply of the tumor had been interrupted. There was then a precipitous fall to 90 and then to 70 mm. Hg. systolic. At this point, the blood was pumped in rapidly and five minims of neosynephrine were given intravenously. The blood pressure rapidly rose to 170 and then gradually declined again. An additional three minims of neosynephrine were then given with elevation to over 100 mm. Hg. for the duration of the closure; however, upon return to his bed, there was another fall in pressure to 40 mm. Hg. systolic, and neosynephrine was again given with effect. During the next six hours, three minims of neosynephrine were given subcutaneously on two separate occasions to control depressions of pressure below 70 mm. Hg. systolic. The pressure then remained stable at 70 mm. Hg. systolic for the following 24 hours after which time it rose

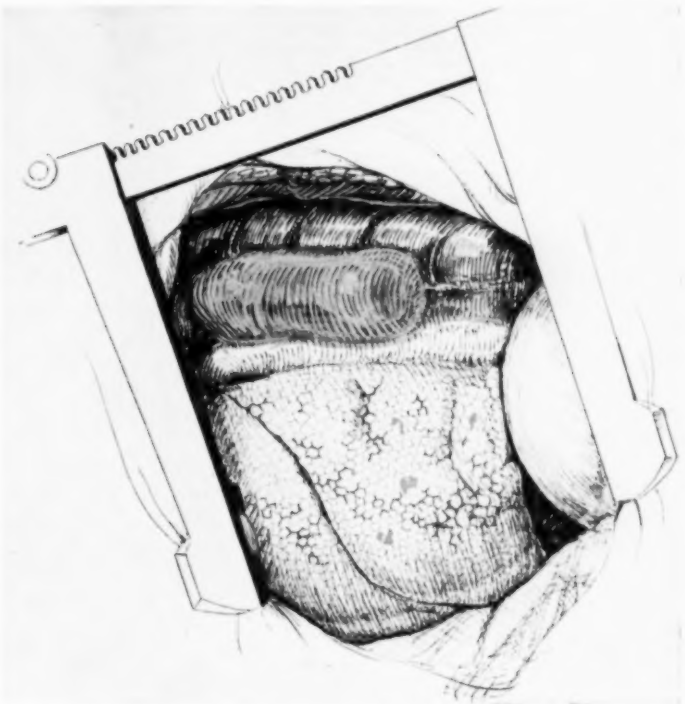

FIGURE 2

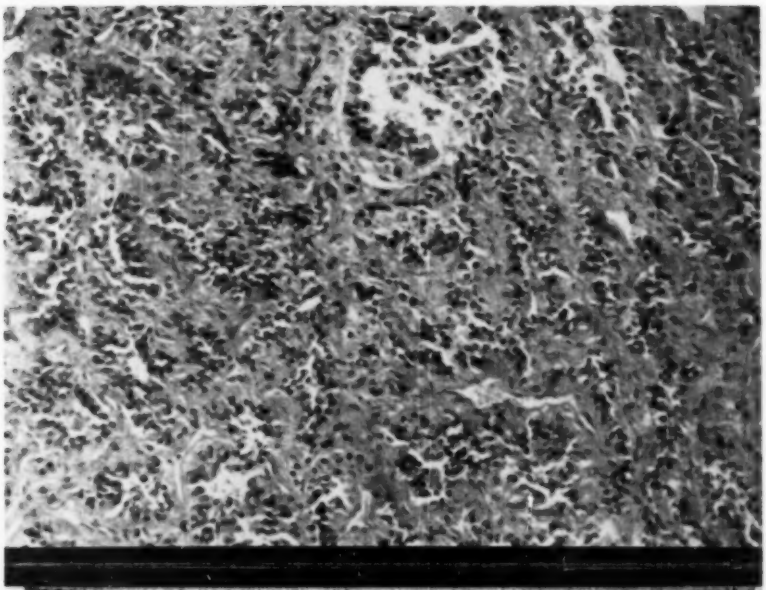

FIGURE 4

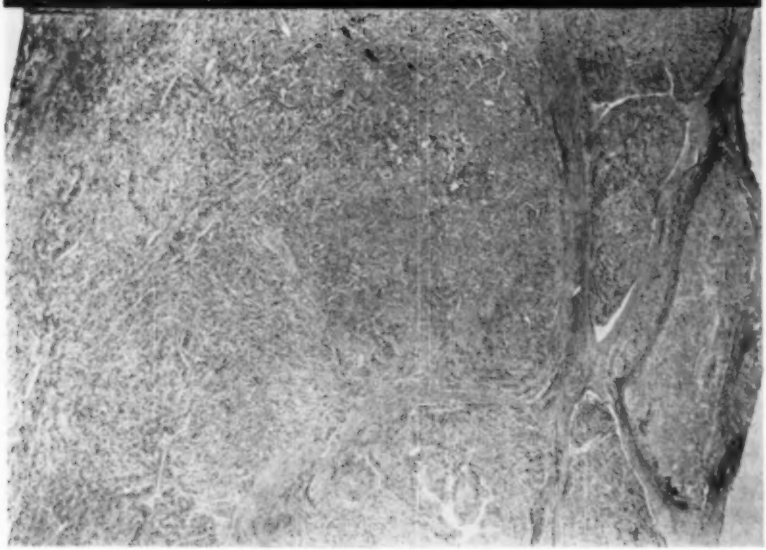

FIGURE 3

to 100 to 110 mm. Hg. for the remainder of his hospital stay. No further complications developed, and he was discharged 10 days postoperatively. On July 22, he was again examined at the office at which time his blood pressure was 120/80 and he was asymptomatic.

Operative Findings and Procedure: The pleural space was free of adhesions. The lung, diaphragm, and mediastinal structures were not remarkable except for the presence of the tumor. This was immediately apparent lying half on the fourth, fifth, sixth and seventh vertebral bodies and half on the adjacent rib heads. It was in line with the sympathetic chain which could be seen to disappear into it from above and emerge from it below. The overlying pleura was white and slightly thickened, but when this was incised and reflected, the tumor itself was found to be covered by an extremely thin layer of areolar tissue. It was slightly lobulated, soft, and grayish-purple in color (Fig. 2). When the pseudocapsule was ruptured, the tumor extruded from the opening as a granular friable homogenous mass. It was extremely vascular. It did not invade the vertebral bodies or the ribs, but tended to bulge into the intercostal spaces. No true invasion was evident. The intercostal vessels and nerves of the corresponding ribs emerged from the lateral and deep aspect of the tumor, and the vessels gave off numerous branches to the tumor.

The thickened pleura overlying the tumor mass was incised and the margins reflected. It was impossible to manipulate the mass without rupturing the thin areolar covering. The sympathetic chain was divided one cm. below the mass and, starting from below, the tumor was dissected from its bed, using sharp and blunt dissection. A considerable amount of blood was lost during the procedure because of the extreme vascularity of the pedicle and the high blood pressure. The tumor had to be "wiped" off the intercostal structures, and there was no apparent capsule or membrane intervening between the tumor and these structures. After all the vessels supplying the tumor had been divided, the sympathetic chain was divided just above the mass, and the excision thus accomplished. It was thought that all the tumor tissue had been removed. It was necessary to insert a small amount of oxidized cellulose into the fifth interspace to aid in the control of oozing in that situation. Because the tumor was so definitely arising from the sympathetic ganglionic chain, it was not thought likely that it was metastatic in origin. Therefore, no attempt was made to open the diaphragm and palpate the adrenal gland on that side. The wound was closed in the routine fashion, leaving one catheter intrapleurally to aid in the re-expansion of the lung. The patient received 1500 cc. of blood throughout the procedure.

Pathological Examination

Grossly the specimen, weighing 50 grams, had an irregular, but smooth surface. It measured 5.0 x 4.5 x 4.0 centimeters. Closely adherent to one surface, was a white membranous tissue 4.0 x 4.0 cm. and 0.2 cm. in greatest thickness. The tissue of the main mass, while mottled yellow-gray to dark red, was otherwise homogeneous and had a uniform, moderately firm consistency. A dark red lymph node, 0.4 cm. in diameter, was also received.

Portions of the tumor were fixed in Zenker's solution and 10 per cent formalin. Eosin-methylene blue, Giemsa, phosphotungstic

acid hematoxylin, Verhoeff elastic tissue, and Goldner's modification of Masson's trichrome stain were used.

Microscopically, the tumor was a homogeneous structure (Figs. 3 and 4), being composed of small, irregular collections of cells which often tended to arrange themselves in a pseudo-glandular pattern. The individual cells were irregularly sized, mostly about 20 micra in diameter, and irregular in shape, varying from polygonal to elongate. The cytoplasm was quite uniformly finely granular and usually acidophilic, but some cells contained a few, or many, similarly sized granules which were light green-brown. Most nuclei were about 10 micra in diameter, round and vesicular, but hyperchromatism was common and larger, irregular nuclei were not rare. No nucleus was found in mitosis. The stroma was scanty, but markedly vascular with innumerable, small, endothelial-lined spaces. Many of the cellular collections mentioned above lay directly against such an endothelial-lined space. No growth of tumor within vessels was found. The capsule for the most part was distinct and fibrous; but in some places, the tumor was growing within it. Alongside the capsule was a moderate-sized nerve which was intermingled with the capsular connective tissue, but it did not enter the tumor proper, nor were other nerves found within the substance of the tumor.

A small lymph node accompanying the specimen was negative.

Pathological Diagnosis: Pheochromocytoma.

Comment: The presence of the tumor growing within the capsule suggested local malignant change. There were, however, no other microscopic criteria indicating cancer.

Although the presence of epinephrine within the tumor was not demonstrated by bioassay, the microscopic appearance in association with the clinical features as outlined constitute sufficient evidence that this was a true pheochromocytoma with the ability to produce epinephrine.

Discussion

Elsewhere than in the thorax, the difficulty in diagnosis lies in the demonstration of the tumor mass. The patient generally has a hypertension of paroxysmal or persistent type in association with symptoms, such as headache, palpitation, rapid pulse, heat intolerance, excessive sweating and nausea. Where the tumor is thoracic in position, the problem is reversed since the mass is readily demonstrated by roentgenogram and there may be neither symptoms nor hypertension. If hypertension exists prior to operation in association with a mediastinal tumor mass, and especially if this is paravertebral in location, then tests with benzodioxan[2] or dibenamine[3] will lower the blood pressure if its elevation is due to excess

epinephrine. Should the hypertension be paroxysmal in type and in the temporary absence of an elevation, these drugs will be of no value and an attempt to demonstrate a hyper-reactor response of the blood pressure by the histamine test,[4] mecholyl test[5] and the cold pressor test should be made. Unfortunately, such a response is accompanied by the unpleasant symptom of a typical hypertensive episode. If no hypertension exists, it is unlikely that the correct diagnosis will be suspected and that attempts to provoke the hyper-reactor response will be carried out. In such a situation, it will probably be the manipulation of the tumor during its removal or, as in the case here reported, the effect of epinephrine or a related drug during the procedures of anesthesia or surgery that will provoke the response that will suggest the diagnosis.

The importance of establishing the diagnosis is more than academic since the patient may die during the acute hypertension produced during the surgery or during the phase of severe hypotension following occlusion of the vascular supply to the tumor. Ewert[5] states that this is the more dangerous period. Where the lesion is a malignant one, the usual hazards of recurrence exist.

The dangers of marked variations in the blood pressure may be largely averted by the use of two drugs: benzodioxan (2-[1-piperdylmethyl]-1, 4-benzodioxan) and dibenamine (dibenzyl-beta-chlorethylamine hydrochloride). Benzodioxan is an epinephrine antagonist and if given intravenously to a patient with hypertension due to epinephrine will result in a marked fall in blood pressure for approximately 15 minutes. If marked hypertension develops during the operative removal of the tumor, this drug may be given to combat the rise in pressure. It may not, however, be effective (2-case No. 2). Dibenamine is an adrenolytic drug[3] and may block the hypertensive effects of a pheochromocytoma for approximately 24 hours after intravenous administration. This can be of diagnostic value in a case exhibiting hypertension and may be of distinct value in the control of blood pressure variations throughout surgery.

If an unusually high elevation of the blood pressure during surgery is the first indication of the diagnosis and neither benzodioxan nor dibenamine is available for control of the rise, then every effort should be made to control the vascular supply to the tumor before it is manipulated in any way. This will not always be possible. After the blood supply has been interrupted and the blood pressure has fallen or is falling precipitously, either epinephrine or neosynephrine can be used intravenously to support the circulation. According to Cahill[2] and as exemplified by the case reported herein, there is a gradual return to normal and it is unlikely that artificial support of the blood pressure will be necessary

after the first 24 hours. Since both adrenal glands are present, adrenal insufficiency will not present a problem.

SUMMARY

1) The occurrence of an intrathoracic pheochromocytoma is reported. This represents the fourth such case on record in the literature.

2) The diagnostic problems, the dangers to be anticipated, and the management of both are briefly outlined.

RESUMEN

1) Se refiere el hallazgo de un caso de pheocromocitoma. Este es el cuarto caso relatado en la literatura.

2) Brevemente se presenta el problema diagnóstico, los peligros posibles y el tratamiento.

REFERENCES

1 Hollingsworth, R. K.: "Intrathoracic Tumors of the Sympathetic Nervous System," *S., G. and O.*, 82:682, 1946.
2 Cahill, George F.: "Pheochromocytomas," *J.A.M.A.*, 138:180, 1948.
3 Spear, Harold C. and Griswold, Dwight: "The Use of Dibenamine in Pheochromocytoma," *New England Med. J.*, 239:20, 1948.
4 Roth, G. M. and Kvale, W. F.: "Tentative Test for Pheochromocytoma," *Am. J. Med. Sci.*, 210:653, 1945.
5 Ewert, E.: Discussion of paper by Cahill. (See Reference 2).

Metastatic Tumors of the Lung*

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From a clinician's viewpoint, carcinomatous pulmonary metastases are still discouraging entities. With the remarkable strides in producing regressive changes of metastatic breast and prostatic carcinoma with hormonal therapy, and the ever widening vista of therapeutic results with artificial radioactive substances, it behooves all of us to re-examine our fundamental knowledge of pulmonary metastases. All too often we become pessimistic about carcinoma and especially about metastases, not realizing that we must be soundly prepared in our diagnostic approach to these conditions for the time when we will have sounder therapeutic aids to handle these overwhelming conditions. It is almost heresy to say today that results may be anticipated in pulmonary metastases. Yet, all of us recall that only a short time ago subacute bacterial endocarditis, pneumococcal meningitis, congenital cardiac disorders, pulmonary carcinoma and a horde of other fatal diseases were considered incurable. Now these are being treated with astonishing success in all centers of the world. Can we then dismiss pulmonary metastases with littel foresight? Or shall we examine closely the etiologies, avenues of transmission, clinical and roentgen manifestations of pulmonary metastases and then cautiously approach and await potential strokes of repair?

The question frequently arises, how often do primary lesions of the various organs metastasize to the lung? In an extensive review of over 1300 cases, Turner and Jaffe[5] list the incidence of lung metastases as in Table 1.

Thus it may be said that the relative frequency of metastases to the lung from malignancies of all organs is approximately 25 per cent. In more simple terms, if a patient has a malignancy there is one chance out of four that he or she will have pulmonary metastases. Further, using rough percentage figures, all neuromuscular, skeletal, glandular, and hemopoietic primary malignancies metastasize 50 per cent of the time. All urinary tract, male and female genital organs, gastrointestinal, and respiratory tract

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lesions metastasize to the lung 25 per cent of the time, and the oral cavity malignant lesions metastasize 10 per cent of the time. (Table 2, Fig. 1).

Next, we must examine the fundamental pathology that occurs in pulmonary metastases. Tumor metastasis, is the translocation of cancerous cells to others parts of the body. The avenues of transmission are principally three: (1) the vascular circulation,

TABLE 1

Review of 1306 Necropsies Showing Incidence of Lung Metastases (After Turner and Jaffee[5])

No. of Autopsies	Systems	Lung Metastases Per cent
185	Urinary tract and male genital organs	28.1
160	Female genital	23.1
218	Oral cavity	11.9
391	Gastro-intestinal tract	20.5
96	Respiratory	28.1
58	Neuromuscular and skeletal	48.2
195	Glandular and hemopoietic	49.7
Total 1303		26.6 Average

TABLE 2 (Summary of Table 1)

Site of Origin	Pulmonary Metastases (Approx.) Per cent
Neuromuscular, skeletal, glandular, hemopoietic	50
Urinary tract, male and female genitals, G. I. and respiratory	25
Oral cavity	10

TABLE 3

Avenues of Metastases

The Circulation:
1. General venous system.
   a. Systemic — bones, kidneys, etc.
   b. Portal — stomach, colon, etc.
2. Vertebral vein plexus.
   a. Prostate, etc.

The Lymphatics (Breast, carcinoma of stomach):
1. Thoracic duct and cisterna chyli.
2. Right lymphatic duct.

Membranous Surfaces:
1. Peritoneum, etc. — carcinoma of ovary.
2. Organs — carcinoma of bladder.

(2) the lymphatics, and (3) the membranous surfaces (Table 3).

The Circulation: Emboli of malignant cells carried by the blood stream are common, especially in highly vascular tumors and those which tend to invade blood vessels. The tumors associated with the systemic circulation (bones, kidneys, etc.) tend principally to invade the lungs, while those in the portal circulation (stomach, colon) tend to mestastasize to the liver.

The Lymphatics: Carcinoma cells tend to grow into the connective tissue spaces and to invade the lymphatics. This may occur by permeation of lymphatics (a method of spread seen in cancer of the breast) or by lymphatic emboli, as in secondary growth in regional lymph nodes (e.g. cancer of the stomach may metastasize to the supraclavicular lymph nodes).

The Membranous Surfaces: Secondary carcinomatous growths may scatter over a serous or a mucous surface and gain a strong foothold in the area surrounding the primary growth. An example is the implantation of the surrounding peritoneum in a carcinoma of the ovary.

If we understand these three fundamental principles of metastasis, we can immediately anticipate the roentgen manifestations

METASTASES TO LUNGS

(From All Organs)

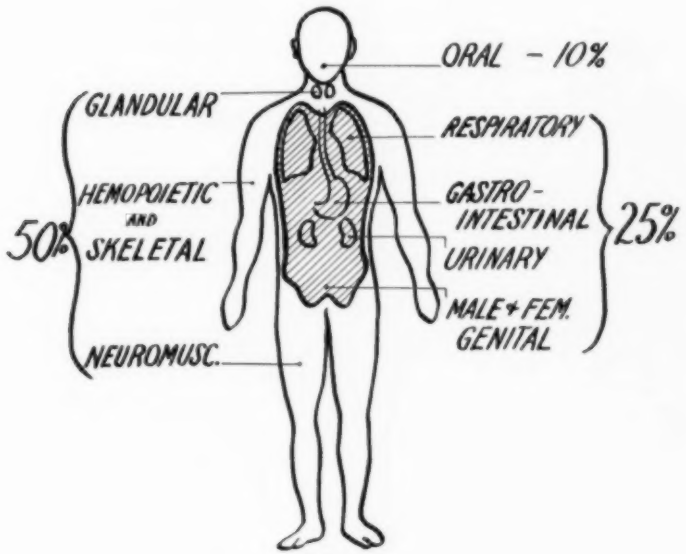


FIG. I

of pulmonary metastases. Characteristic patterns can therefore be anticipated in blood-borne, lymphatic disseminated, and membranous surface extension types of metastases.

The Roentgen Patterns of Pulmonary Metastases

A. *The Circulatory Pattern (Hematogenous Metastases):* The route of hematogenous metastases is through the veins. Certain lesions (e.g. sarcomas and carcinomas of the kidney) spread principally by this method. Tumor cells may grow into a vein, form a thrombus, and then disperse tumor emboli. These tumor emboli reach the right heart and then enter the lung via the pulmonary arteries. Here the characteristic circulatory pattern of a metastasis will be produced. From the lung, tumor cells may invade the pulmonary veins, destroy them and thus reach the left side of the heart and systemic circulation.

Of extreme interest is the phenomenon of systemic metastasis without lung metastases. For example, a carcinoma of the prostate will frequently metastasize to the bones, yet repeated careful examinations will reveal no evidence of metastases to the chest. This phenomenon is now adequately explained by Batson's[1] studies of the vertebral vein plexus. This plexus has no valves and communicates with the other main systems (Fig. 2). When pressure changes occur within the abdominal or pleural cavity, retrograde

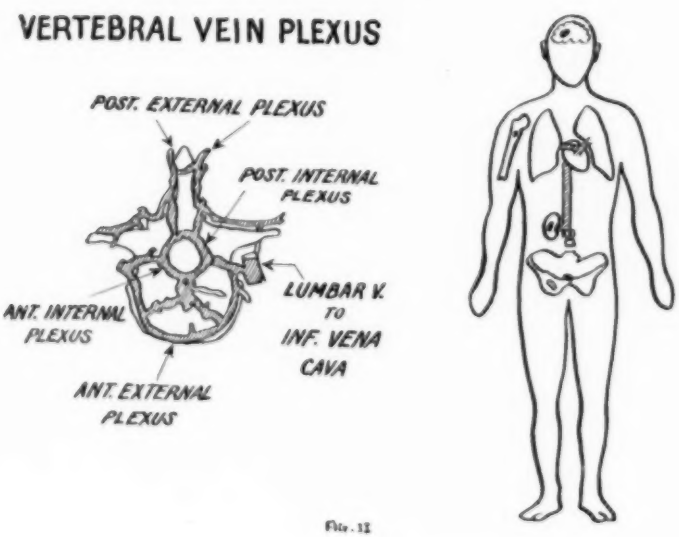


Fig. 11

flow of carcinoma cells takes place through these veins without valves producing metastases to unexpected organs. It has been shown by this method that when opaque material is injected into the dorsal vein of the penis, it can reach the vertebral system without first entering the pulmonary circulation. Thus carcinoma of the prostate may reach the vertebrae, pelvis and upper ends of the femur without evidence of disease in the lungs. Also with cough, a carcinoma of the lung located in the area of the posterior bronchial vein, may metastasize through this vein into the vertebral vein plexus and thence to the brain, without evidence of pulmonary metastases.

In the hematogenous pulmonary metastases the rich capillary network in the lungs filters out the tumor cells reaching this organ. This filtering mechanism gives rise to two main types of metastatic lesions: (1) the solitary nodular shadow and (2) the multiple nodular shadows. These in turn may vary all the way from "miliary" deposits to the huge, so-called, "cannon-ball" metastases. We may then classify hematogenous metastases as follows:

Solitary Nodular Shadow:
1. Small type (Figure 3).
2. Large type (Figure 4).

Multiple Nodular Shadows:
1. Miliary type (Figure 5).
2. Small nodular type (Figure 6).
3. Large nodular type.
4. Huge nodular or "cannon-ball" type (Figure 7).

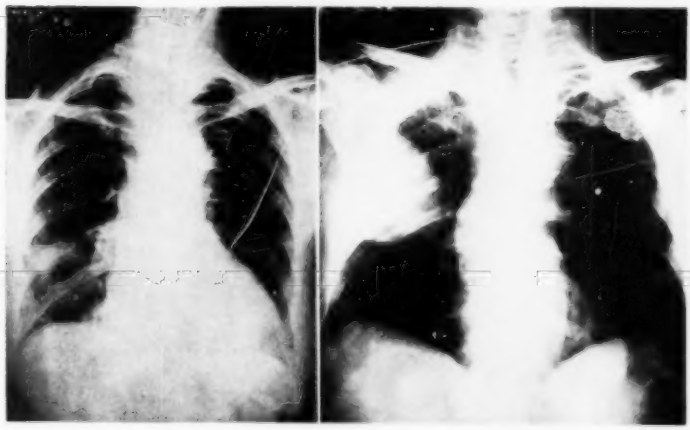


FIGURE 3 FIGURE 4

Fig. 3: Solitary Nodular Shadow—Small Type.
Fig. 4: Solitary Nodular Shadow—Large Type.

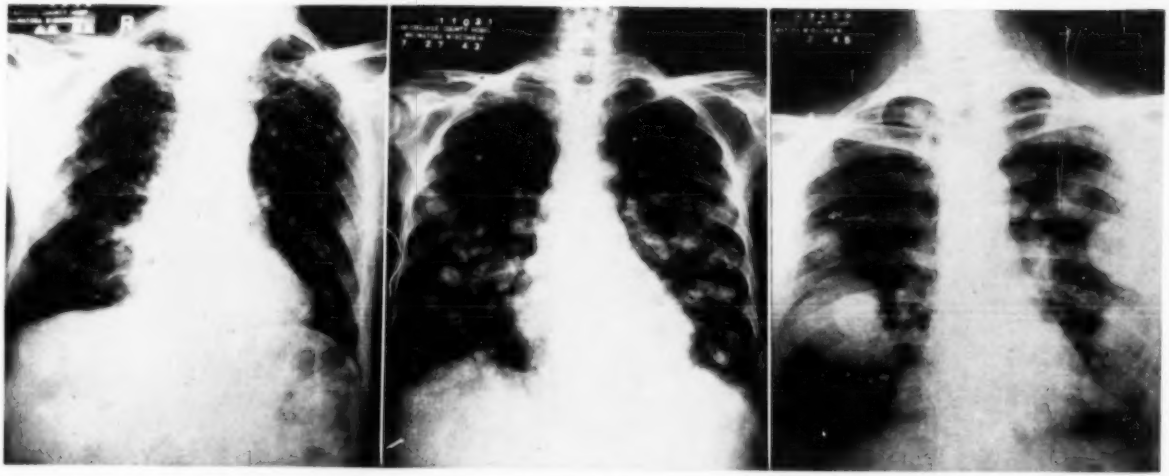


FIGURE 5 FIGURE 6 FIGURE 7

Fig. 5: Multiple Nodular Shadows—Miliary Type.

Fig. 6: Multiple Nodular Shadows—Small Nodular Type.

Fig. 7: Multiple Nodular Shadows—"Cannon-Ball" Type.

The solitary nodular metastasis is perhaps the most difficult pulmonary lesion to differentiate and the list in Table 4 is an indication of the multiple lesions which can stimulate this particular finding.

With such an imposing array of lesions, it is no wonder that the roentgenologists and chest men throw up their hands in despair when a solitary nodular lesion appears on a film. Yet, if we will follow a certain routine procedure in the presence of a solitary nodular shadow, rather than "guess" at the possibility, we may arrive at the correct diagnosis more frequently than anticipated. Table 5 is an all inclusive procedure to follow for the differential diagnosis of the solitary pulmonary nodule.

Multiple nodular metastases may vary, as described, from the minute almost pin-point lesions to the huge "cannon-ball" type. Miliary hematogenous metastases is usually referred to as "miliary carcinosis" and presents sometimes an extremely difficult differential diagnosis from miliary tuberculosis and pneumoconiosis. Miliary tuberculosis, however, changes fairly rapidly and serial films will distinguish it from the carcinomatous lesion. Pneumoconiosis, on the other hand, will show no change over a long period of time as compared to miliary carcinosis, and further, the history of exposure will aid in the differential diagnosis.

In turn, a wide host of conditions will simulate the multiple

TABLE 4

Differential Diagnosis of a Solitary Pulmonary Nodule

I. Chest Wall:
Nevi, nipple shadow, rib neoplasm and nerve root neoplasm.

II. Mediastinum:
Dermoids, teratomas, thymic neoplasms, esophageal diverticula, diaphragmatic hernia, neurofibroma, ganglioneuroma, dumbell lipoma of pericardium.

III. Pleura:
Benign tumors (fibroma, lipoma).
Malignant tumors (fibrosarcoma).
Loculated effusions.

IV. Lungs:
Primary malignancy — Carcinoma, Sarcoma, Chorionepithelioma.
Benign — Chondroma, Adenoma of bronchus.
Inflammatory — Nodular Tuberculosis, Abscess, Segmental pneumonia, Mycotic, Gumma.
Cysts — Congenital fluid, Echinococcus.
Foreign bodies —
Interbronchial Lymph Nodes — Tuberculosis, Hodgkin's disease, Lymphosarcoma.

TABLE 5

Routine Procedure for Differential Diagnosis of the Solitary Nodular Shadow

1. Examine patient:
   Clinical survey (rectal, prostate, temperature, blood count, etc.)
   (exclude naevi, nipple shadows, etc.)
2. Stereoscopic roentgenograms:
   Exclude the chest wall and pleural lesions.
3. Lateral and oblique roentgenograms:
   Determine position of lesions — anterior (dermoids, thymus, etc.)
   posterior (ganglioneuromas, neurofibroma, etc.)
4. Antero-posterior Bucky chest films and tomographs:
   Calcification — dermoids, nodular tuberculosis.
   Cyst wall — Echinococcus disease, congenital cysts.
5. Routine bone films:
   Lateral skull, ribs, dorso-lumbar spine, pelvis, humeri, femurs.
   Exclude osseous metastasis.
6. Esophagram and complete gastrointestinal and gall bladder studies:
   Diverticula, diaphragmatic hernia, primary carcinoma.
7. Sputums and gastric specimens:
   Tuberculosis, mycoses, bacterial pathogens, tumor cells.
8. Bronchoscopic examination (with aspiration for smear and culture):
   Foreign bodies, primary neoplasms, inflammatory lesions.
9. Systemic tests:
   Pyelograms and others.
10. Exploratory thoracotomy.

TABLE 6

Differential Diagnosis of Multiple Nodular Shadows

Miliary Shadows:

1. Miliary tuberculosis.
2. Boeck's sarcoid.
3. Miliary carcinosis.
4. Hyphomycetosis.
5. Bronchiolitis.
6. Pneumoconiosis.
7. Congestion.

Large Nodular Shadows:

1. Metastatic neoplasms of lung.
2. Metastatic neoplasms of pleura and ribs.
3. Multiple echinococcus cysts.
4. Bronchogenic tuberculosis.
5. Infarcts.
6. Suppurative and gangrenous bronchopneumonia.
7. Metastatic lung abscesses.
8. Coccidioidomycosis.
9. Tularemia.
10. Hematogenous pneumonia.

nodular metastases. Table 6 will aid in considering some of the lesions producing similar roentgen shadows.

B. *The Lymphatic Pattern (Lymphangitic Metastases):* To fully understand lymphangitic metastases a fundamental knowledge of the lymphatic drainage of the body is essential. Two principal routes of lymphatic drainage are present: (1) through the thoracic duct, and (2) through the right lymphatic duct (Fig. 8a).

The Thoracic Duct and cysterna chyli drain the left side of the head, neck and thorax, the left upper extremity, left lung, left heart, and the lower and front part of liver. It also drains the lower limbs, walls and viscera of pelvis, kidneys, suprarenal glands, stomach, intestine, pancreas, and spleen (Fig. 8b).

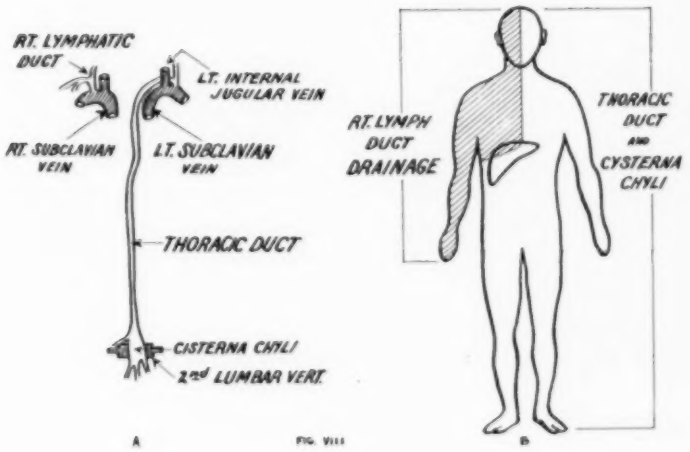
The Right Thoracic Duct drains the right side of the head, neck and thorax, right upper extremity, right lung, right side of heart, and the convex surface of the liver (Fig. 8b).

With these anatomical facts in mind, it is easy to understand the presence of the Virchow node in a carcinoma of the stomach or pancreas, or the presence of metastatic supraclavicular or axillary lymph nodes on the right side in a primary carcinoma of the right lung.

The anatomical lymphatic drainage of the lung is essential to the understanding of the roentgen picture of lymphangitic metastases.

In *each lung* there are three areas of lymphatic drainage: superior, middle and inferior:

LYMPHATIC DRAINAGE IN MAN



Right Lung:

1. Superior area — right laterotracheal nodes.
2. Middle area — right laterotracheal nodes.
   intertracheobronchial nodes.
3. Inferior area — bifurcation nodes.

Left Lung:

1. Superior area — left laterotracheal nodes.
   anterior mediastinal nodes.
   subaortic nodes.
2. Middle area — anterior mediastinal nodes.
   laterotracheal nodes.
   bifurcation nodes.
3. Inferior area — bifurcation nodes.

The *lymphatics of the parietal pleura* are divided into those of the diaphragm and the thoracic wall. The lymphatics of the diaphragm empty into the lateral precardiac and anterior mediastinal nodes on the *left*, and the posterior mediastinal on the *right*. The *posterior portion of the diaphragm* connects with the subperitoneal infra-diaphragmatic lymphatics which terminate into the abdominal para-aortic nodes. They are also in communication with the lymphatics of the liver, adipose capsule of the kidney and the suprarenal gland. The *thoracic pleural* lymphatics are in three regions: (1) from 1st rib to pleural dome, (2) 2nd to 4th rib, and (3) 4th to 6th rib.

Roentgenologically, lymphangitic carcinoma shows a diffuse, string-like formation of increased density, which radiates from the hilum to the periphery.[3] The design is more marked in the central and basal portions of the lung but may extend into the

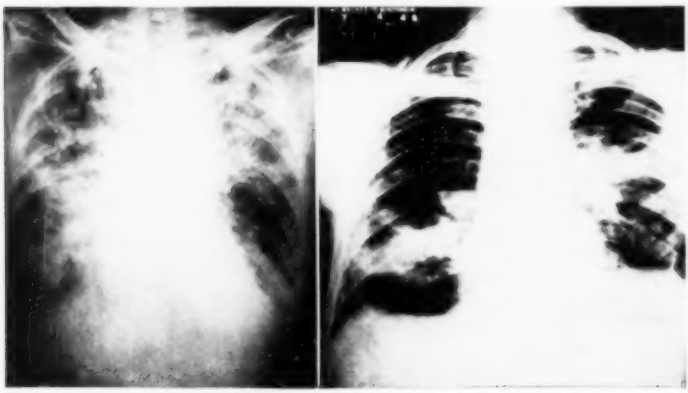


FIGURE 9 FIGURE 10

Fig. 9: Lymphangitic Pulmonary Metastases—Diffuse "String-like" Formation.
Fig. 10: Lymphangitic Pulmonary Metastases—Matted Irregular Type.

periphery and also the upper portions. If it arises from an intrapulmonary tumor, the lymphatic spread may be unilateral. The fine string-like formations may give rise in certain areas to a "matted irregular appearance" or to numerous adjacent miliary nodules (Figs. 9 and 10).

The differential diagnosis of intra-pulmonary lymphangitic carcinoma is as follows:[3]

1. Miliary tuberculosis—hilar shadows less dense, upper portions involved.
2. Pulmonary congestion and edema.
3. Pneumoconiosis—history of exposure.
4. Sarcoid—sharply defined hilar masses.
5. Fibrosis with emphysema.
6. Bronchiectasis—long history.
7. Atypical pneumonia—history.

SUMMARY

The various forms of pulmonary metastases are presented, (1) the circulatory, (2) lymphatic, and (3) membranous surface extensions. The differential diagnosis of pulmonary metastases on the roentgenograms are described and methods utilized to differentiate the lesions are explained. The incidence of pulmonary metastases from all organs is discussed. The present-day concept of osseous and systemic metastases without pulmonary metastases is presented.

The author wishes to thank Dr. Saul L. Parks, senior resident in Radiology, Milwaukee County Hospital, for his help in the preparation of this manuscript.

RESUMEN

Se han presentado las diversas formas de tumores pulmonares metastáticos, (1) circulatorios, (2) linfáticos y (3) extensiones de las superficies membranosas. El diagnóstico diferencial de las metástasis pulmonares en las radiografías se describe y se explican los métodos empleados para diferenciar las lesiones. Se discute la frecuencia de las metástasis pulmonares a partir de todos los órganos. El concepto actual de las metástasis óseas y de sistemas sin metástasis pulmonares se presenta.

REFERENCES

1 Batson, O. V.: "The Vertebral Vein System and Mechanism of the Spread of Metastases," *Am. J. Roentgenol.*, 48:715, 1942.
2 Culver, G. J.: "Miliary Carcinosis of the Lungs Secondary to Primary Cancer of the Gastro-Intestinal Tract," *Am. J. Roentgenol.*, 54:474, 1945.
3 Golden, Ross: "Diagnostic Roentgenology," Vol. I. New York, *Thomas Nelson and Sons*, 1945.
4 Mueller, H. P. and Sniffen, R. C.: "Roentgenologic Appearance and Pathology of Intrapulmonary Lymphatic Spread of Metastatic Cancer," *Am. J. Roentgenol.*, 53:109, 1945.
5 Turner, J. W. and Jaffe, H. L.: "A Clinical and Roentgenological Study of Involvement of Skeleton and Lungs," *Am. J. Roentgenol.*, 43:479, 1940.

Forty Years' Experience with Artificial Pneumothorax*

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It is obviously impossible to compress into 20 minutes 40 years experience with a medical subject as vital as artificial pneumothorax and about which there have developed over the years so many controversial views. I shall therefore only endeavor to state briefly my own views arrived at from experience in treating tuberculosis, before and since artificial pneumothorax was introduced.

From 1905 until the advent of relaxation therapy I walked the wards of White Haven Sanatorium, the Henry Phipps Institute and the Tuberculosis Division of the Jewish Hospital and helplessly watched most of the unfortunate victims of this dread disease slowly and inevitably waste, burn up and die. It was this feeling of helplessness and riding in the face of certain defeat which stimulated my interest in a report by Forlanini of 25 cases treated by artificial pneumothorax published in 1906.

My first pneumothorax was administered in 1908 on a patient in the White Haven Sanatorium. This was the first attempt at treating tuberculosis by artificial pneumothorax in Pennsylvania. The technique described by Forlanini was followed. I had to build my own apparatus. There was no x-ray or fluoroscopic equipment. The patient was a young man named Cohen. He developed a pneumonic spread to the contralateral lung and died but we had no necropsy.

My second attempt was in 1910—shortly after the Eagleville Sanatorium was opened. From 1910 until 1919 about 20 patients were treated with two deaths from air embolism. Still no x-ray machine or fluoroscope was available, but I did abandon the Floyd Robinson trocar and cannula.

In 1923 we got an x-ray apparatus; a year later a fluoroscope was purchased and this marked the dawn of a new era for me. It wasn't until then that I had the vaguest notion of what a lung looked like under pneumothorax treatment. Lungs appeared like sausages pressed up against the mediastinum. Airless lungs, the

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size of a fist, pushed into the upper part of the chest or suspended from spindly adhesions looking like a hornet's nest, were seen. Fluid was observed in various amounts where it was not suspected but some nice selectively relaxed lungs and not a few reasonably good relaxations were also seen.

In 1924 while visiting Davos, Switzerland, the mecca for tuberculosis—"The Magic Mountain" of Thomas Mann, I saw beautiful hospital buildings much like the grand hotels de luxe of Continental Europe set on the mountain sides amid pine forests basking in the glow of the Alpine sun. Everybody in Davos was doing artificial pneumothorax with confidence and enthusiasm. I talked to Dr. Schreiber who had already reported 100 thoracoplasties and visited with Dr. Sauerbruch in Munich who had done 700 thoracoplasties. Not a single thoracoplasty had been reported from Philadelphia at that time and only 110 cases had been described in the literature of the United States and Canada (56 of these were credited to Dr. Archibald of Montreal).

On returning home determined to pursue and push the surgical treatment of tuberculosis and to develop the means with which to do it, not much help was received from the local medical profession. While seeking a surgeon, my friend Dr. John B. Deaver, literally threw up his hands and said "No, A. J. I am too old to delve into this new field—get a young man." Dr. John Gibbon suggested his young assistant Dr. John B. Flick and a happier proposal could not have been made. Dr. Flick spent months in careful preparation and study and before the year was over he did a thoracoplasty at the Pennsylvania Hospital on an Eagleville patient, the first done in Philadelphia. This patient is living and well today after 25 years of useful, and happy service as a technician in one of our important medical research institutions. For the next three years Dr. Flick continued to do our surgery at the Pennsylvania Hospital with marked success and the fine work done by him in this new and virgin field laid the basis for thoracic surgery in this part of the country.

In 1926, 100 cases treated with artificial pneumothorax were reported. Even under those dark hit-or-miss conditions I was able to report 50 per cent satisfactory results in a series of cavernous cases—40 per cent of whom were in the moderately advanced and 60 per cent in the far advanced stage of the disease.

It was soon realized however that in order to do pulmonary surgery effectively it was necessary to have the proper hospital facilities at the sanatorium; that shuttling the patients from the sanatorium to the city and back, though the distance was not great, was not entirely satisfactory.

It would be interesting to relate here the campaign for a million

dollar hospital for Eagleville but time does not permit. Suffice it to say that in the fall of 1927 we opened at Eagleville a 70-bed hospital—a fireproof steel structure with all the facilities and equipment for surgery. When the hospital was completed all surgical activities were transferred to the sanatorium. For several years Dr. Flick continued his excellent work and then turned it over to his able assistant Dr. George Willauer our present thoracic surgeon.

For the past 20 years from 70 to 80 per cent of our patients have been getting some form of surgery, designating artificial pneumothorax as surgery, and all accepted surgical procedures are used. The treatment to be pursued in each case is decided at staff conferences after careful consideration of complete x-ray, clinical and laboratory studies. The surgical procedure decided upon is the result of the combined judgment of the entire medical staff. This has been going on for 22 years in an institution with 200 patients.

The above indicates the background of my experience and emphasizes that I have always been an enthusiast for pulmonary surgery and not just pushing or promoting a single operation to the exclusion of all other surgical procedures. I am indeed mindful of the value of phrenic nerve interruption, thoracoplasty, pulmonary resection and pneumoperitoneum—they all have their appropriate place in the treatment of tuberculosis but it is my firm conviction that artificial pneumothorax is beyond doubt the brightest jewel in the crown of pulmonary surgery.

That artificial pneumothorax has a definite place in the treatment no experienced phthisiologist can deny. There is however considerable difference of opinion as to its value compared to other surgical procedures and it seems to me that in the last several years artificial pneumothorax has been put on the defensive without good reason. It is the best form of relaxation therapy in properly selected cases and is indicated in the largest proportion of cases in the average sanatorium population. It is a simple harmless procedure in the hands of an experienced physician who has learned the proper technique. Simple as it is however it is not an operation to be thrown to the resident. It is not merely a needle pushing job and should not be done in the home as a specific treatment for tuberculosis. It is part and parcel of the sanatorium regimen and is not a substitute for sanatorium treatment. I haven't done pneumothorax or even a refill in the patient's home in 25 years. My pneumothorax patients are kept in bed at complete rest in the sanatorium until they meet all the criteria for getting up, applied to the non-pneumothorax cases. Each case is fluoroscoped every week and a sketch of the fluoroscopic image is drawn on a special sheet kept as part of the record. No pneumo-

thorax case is discharged from the sanatorium until he has met all the requirements for an "apparently arrested case" and he comes to the Eagleville clinic in the city or the sanatorium for his refills where we have exactly the same surgical and x-ray layout and equipment that we have in the sanatorium.

Pneumothorax is not a competitor of thoracoplasty or any other surgical procedure but whereas thoracoplasty is applicable to about 10 per cent of the average sanatorium population, pneumothorax is applicable to about 50 per cent and it is my conviction that in the career of every patient there was a time when he was a suitable case for pneumothorax and could have gotten well without the need for more formidable surgery. Much has been said and written about the dangerous complication of artificial pneumothorax. A spot check on May 1 of my 78 current cases revealed seven with a little fluid in the sulcus, less than 10 per cent and only two had enough fluid to warrant aspiration in the past six months. Among these 78 cases there were nine getting bilateral pneumothorax not one of whom had fluid.

An operative death has not occurred in 23 years. Pneumolysis is not encouraged. Adhesions are not cut if a good functional pneumothorax is obtained unless the adhesion is actually holding out the cavity. So many cases have gotten completely well without ideal collapse of the lung that I do not rush into the Jacobeus procedure. With a good cushion of air between the chest wall and the lung relieving the peripheral pull and affording pulmonary relaxation satisfactory results are obtained in the presence of adhesions. In my present series of cases eight had pneumolysis and two of these developed empyema.

Upon the proper selection of cases will largely depend the outcome. The ideal case is one with an early progressive thin-walled cavernous lesion situated in the upper lobe or the apex of the lower lobe. From here it is easier to designate those cases that are not suitable: (1) Old thick-walled large cavities wherever situated; (2) Cavities in the hilar region; (3) Basal cavities; (4) Caseous pneumonic lungs; (5) Atelectatic lungs; (6) Advanced bilateral disease with serious constitutional deterioration; (7) Chronic fibroid phthisis; (8) Bronchial tuberculosis. There are exceptions to all of these. My patients usually are kept in bed at least a month, often two before proceeding with artificial pneumothorax.

Discontinue Treatment

A moot question seems to be when to discontinue pneumothorax. The longer my experience with artificial pneumothorax the longer I have been keeping up the refills. I started with six months to a

year; then a year to two years; now it is three to five years. Many of my patients refuse to stop treatment at the end of five years. They feel so confident with it and find that it interferes so little with their normal pursuits that they ask to continue. Ninety per cent of out-patients are gainfully employed and many of the women patients have gone through one or more pregnancies without ill effects while getting pneumothorax. My attitude towards marriage and childbearing has changed completely in the last 15 years. Formerly single women were advised not to marry and the married ones to avoid childbearing. Now, unless there is some special reason, neither of these normal physiological pursuits is opposed.

Technique

The technique is the most important factor in the treatment. No matter how carefully the cases are selected or how well the sanatorium is conducted, if the technique is bad, the results will be bad. In the first place the most scrupulous surgical asepsis should be observed. All kinds of needles and machines have been used and a 20 gauge 2-inch stock needle attached to a three-way adapter and a 2 cc. glass syringe has proved the best combination. A 0.5 per cent novocaine solution is injected through the same needle as the air is introduced. A Robinson machine is used for the initial procedure because the water manometer is more sensitive, but for refills the Zavod machine is preferred. It takes about two minutes for the operation and one minute to change patients, so that 20 pneumothoraces are done in an hour. Small refills at frequent intervals, weekly or bi-weekly are prefered so as to keep the lung in a state of rest. If a large refill is given at long intervals the lung is compressed too much for the first week; starts to expand the second and is almost completely reexpanded by the time another refill is given. This accordion action to which the lung is subjected is not good treatment.

CONCLUSIONS

An attempt has been made to report briefly my personal experience with artificial pneumothorax covering a period of 40 years. My first 16 years may be called the dark era. It was an era of exploration, a period of trial and error. The last 25 years have been illuminating and rewarding. It was the success of artificial pneumothorax that led to the other surgical developments that now crown the achievements of the thoracic surgeon and it was the importance that surgery has assumed in the treatment of tuberculosis that has changed the entire aspect of sanatorium treatment. It has brought the sanatorium down from isolation

on the mountain top to the large cities where the patients come from and the medical talent resides. It has transformed the wooden cottage and the primitive shack into a modern hospital where a team of experts is assembled—a phthisiologist, a thoracic surgeon, a roentgenologist and bronchoscopist who devote their combined talents in the interest of the patient. It has helped to clip the annual death rate from 200 per 100,000 in 1908 to 30 per 100,000 in 1949. And finally, it is my considered judgment that artificial pneumothorax is still the best single procedure in the treatment of pulmonary tuberculosis in carefully selected cases, properly administered and in combination with all tried and effective remedies, new and old.

CONCLUSIONES

He intentado referir brevemente mi experiencia personal con el neumotórax artificial, que abarca un período de 40 años. Mis primeros 16 años pueden llamarse la edad obscura. Fue ésta una época de exploración, un período de prueba y error. Los 25 últimos han sido años de iluminación y recompensa. El buen éxito del neumotórax artificial fue lo que condujo a los otros adelantos quirúrgicos que ahora coronan las proezas del cirujano torácico, y la importancia que la cirugía ha alcanzado en la terapia de la tuberculosis ha sido lo que ha cambiado el aspecto entero del tratamiento sanatorial. Ha trasladado al sanatorio del aislamiento de la cima de la montaña al centro de las grandes ciudades, donde viven los pacientes y reside el talento médico. Ha transformado la casita de madera y la choza primitiva en un hospital moderno donde se reúne un equipo de expertos—un tisiólogo, un cirujano de tórax, un roentgenólogo y un broncoscopista que dedican su combinado talento al provecho del enfermo. Ha ayudado a reducir el índice de mortalidad anual de 200 por 100,000 en 1908 a 30 por 100,000 en 1949. Y, finalmente, mi deliberado juicio es que el neumotórax artificial todavía es el mejor procedimiento en el tratamiento de la tuberculosis pulmonar en casos cuidadosamente seleccionados, cuando se administra apropiadamente y en combinación con todos los otros remedios probados y eficaces, tanto nuevos como viejos.

Discussion

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The excellent paper of Dr. Cohen has rightly emphasized the great value of artificial pneumothorax.

I would like to discuss this subject from the standpoint of re-expansion. The indications for instituting pneumothorax therapy are much more clearly defined than those for discontinuing it. The one positive reason for allowing the lung to reexpand is a healed lesion—but who knows for sure whether it is healed and will stay so? It is for that reason that the doctor hesitates to let the collapsed lung try its wing again and why the patient in agreement wants to let well enough alone. The questionaire sent out by Dr. Edward Hayes revealed the conflicting opinion on re-expansion of pneumothorax and the need for further discussion and evaluation.

This is a situation that is rather unfortunate because it leaves us in the treatment of this disease at a half-way station. To complete the journey back to a normal state we should have a re-expanded lung that will stand the stress and strain of the individuals environment. You are all aquainted with the many factors that make a pneumothorax cavity a potential source of danger. It seems in keeping with the axiom that nature abhors a vacuum. Thus it appears that whenever possible, as judged from the best clinical laboratory and x-ray opinion, a collapsed lung should be made to resume its God-given function and so establish the individual again as a normal psychological person. This should be the goal in pneumothorax therapy. Sometimes, under our present program we attain it; then again we fail but in many instances we neglect to try it. Refills follow refills and the years go by.

The Veterans Administration has a ruling which considers an individual under pneumothorax treatment as 100 per cent disabled. There can be little question but that such a ruling was meant to protect the individual as much as possible from a breakdown. We cannot argue against the good intention of this generous ruling. It seems worthwhile however to comment briefly on the psychological implications of such a rule. A person who is diagnosed as 100 per cent disabled usually becomes 100 per cent disabled in his own mind, from the standpoint of persuing a gainful occupation. It is the rare one that dissents from the majority opinion. One can become totally and even permanently disabled by a ruling or by ones mental attitude. On the other hand we have all seen mentally rugged individualists who in spite of crippling conditions have bravely weathered adversity and carried on in a gainful pursuit.

Recognizing these human reactions and cognizant of the need of helping the pneumothorax patient back to a better life there has recently been established at the Veterans Administration in St. Petersburg, Florida, a collapse therapy board whose function it is to reevaluate at stated intervals the pneumothorax patients with a view to permanent cure.

The Board consisting of two internists, a thoracic surgeon, a chest man and a roentgenologist, review the history, physical, laboratory and x-ray data and then with an opinion from the physician in the field who has cared for the patient, a decision is agreed upon as to ' where to go from here." It is felt that the physician who has given the pneumothorax refills has an important place in this set-up and so his valued opinion is sought in arriving at the proper evaluation. The patient appears before the board and is given to understand that whatever decision is arrived at is made with one purpose in mind and that is his future welfare. It is intended that he again become a functioning and useful citizen. It is interesting to note the respectful enthusiasm of the patient when he is satisfied that this board is eager to help him in his return to gainful living. With this mental attitude he is ready to resume the journey back to a normal life.

Let us keep in mind that pneumothorax therapy has been a great aid to healing a tuberculous lesion, but that until we restore the collapsed lung to its best physiological state we have only half finished the job of treating the patient.

MOSES J. STONE, M.D., F.C.C.P.
Boston, Massachusetts

We have listened to an interesting as well as historical talk. It is rather difficult for me to decide whether Dr. Cohen gave this paper in a vein of reminiscence or has also tried to give us some principles for guidance in carrying out artificial pneumothorax therapy in the year of 1949.

Reminiscence usually conveys a subject of blessed memory hallowed by the passing of time. Pneumothorax therapy however is quite dynamic and therefore should stand the evaluation as well as some appraisal in the general scheme of therapy. Would that we had a whole afternoon for this one subject, as it is vital, is constantly on our minds and we have been woefully shy in its discussion. As a matter of fact, the literature of late on pulmonary tuberculosis has been conspicuous by the absence of critical studies of artificial pneumothorax therapy.

In the few minutes alloted to me, I would like to praise Dr. Cohen for his pioneering work in the active treatment of pulmonary tuberculosis. It took courage and a stout heart to collapse a lung without the aid of past experience and guidance of the modern laboratory and x-ray. Admiring as I do these sturdy pioneering qualities I want, at the same time, to call attention to a few points. There was a time when the terms compression

and collapse therapy might have been used interchangeably. At the present time, I do not condone the word compression in place of collapse when referring to pneumothorax treatment.

I would like also to comment regarding the statement of 50 per cent satisfactory results in cavernous cases. What is the yardstick he uses to appraise? In the long run, I believe that in most hands artificial pneumothorax therapy did not achieve the 50 per cent desirable results. I would add that it can be done if ideal cases were selected and unsatisfactory pneumothoraxes soon abandoned. With meticulous care and proper management of the cases, this figure undoubtedly could be attained. At present, this figure of 50 per cent good results still looms large.

Dr. Cohen also states that for the past 20 years from 70 to 80 per cent of his patients have been getting some form of surgery including pneumothorax. With our aging population in our sanatoria in the New England states, this figure seems rather high. We have been of late, much more cautious with its use, especially with the advent of streptomycin. Many more cases were treated conservatively, especially those over the age of 50 years. We in New England are also not so certain now that artificial pneumothorax therapy is the best form of collapse therapy in the largest proportion of cases in the average sanatorium population. It is not quite as simple a procedure as supposed to be in spite of the simplicity of its technique, and it is certainly not harmless.

Bronchoscopy as a guide in the choice of cases of patients with endobronchial disease should be more emphasized. The speaker mentioned certain contraindications, among these atelectasis as well as hilar and basal cavities. These are usually associated with endobronchial disease and bronchoscopic examinations should be carried out.

I cannot help but take issue also in regard to pneumonolysis. Adhesions do interfere with satisfactory healing although this may not be immediately evident. Cavities may appear to be closed but tomography may prove otherwise. I personally make a plea for severing all adhesions if possible, and if not, abandon the pneumothorax. I too have a great deal of respect for pneumolysis and prefer that when in doubt, they are to be left alone. Thoracoscopy in good hands is fairly harmless, and should be carried out in cases of certain types of pleural adhesions.

I should like to make a plea for meticulous care in carrying out pneumothorax therapy. Many a sin has been committed in the name of pneumothorax therapy. The selection of cases should be most carefully considered. Unsatisfactory pneumothoraces should be abandoned soon, in favor of some other form of treatment. Indefinite length of time in regard to carrying on this

therapy is certainly not scientific. Four to five years should be sufficient in the great majority of cases. Finally I would like to point out that the very simplicity of the technique of pneumothorax therapy is its very liability. It is a procedure fraught with great dangers. In the past 25 years I have learned to approach this form of therapy with respect and frequently with a certain amount of trepidation. My years of experience with pneumothorax therapy have increased this feeling rather than decreased it.

Residual Cavities in Pulmonary Coccidioidomycosis: Follow Up Studies*

RUDOLPH BERKE, M.D., ALEXANDER SCHOMER, M.D. and HYMAN E. BASS, M.D., F.C.C.P.**
New York, New York

In an article published elsewhere[1] we reported observations on 20 cases of residual lesions of pulmonary coccidioidomycosis in veterans of World War II now residing in New York City. Thirteen cases were described in detail. Twelve were of the form known as the initial or primary infection, and one was the progressive or disseminated (coccidioidal granuloma) form of infection. The need for a careful distinction between these two forms has been stressed most recently by Smith, Beard and Saito.[2] The primary form of infection follows the inhalation of the chlamydospores of the fungus coccidioides immitis, and results in self-limited, usually benign, pulmonary lesions. The disseminated form of infection, which is relatively rare, arises from lymphohematogenous spread of the primary infection, and it is fatal in up to 50 per cent of the cases. The high incidence,[3] (estimated 25 per cent), of coccidioidal infection in military personnel who were exposed in the Southwest desert endemic area is reflected in the veterans now coming under medical observation. A significant number of cases of residual pulmonary lesions have been encountered.

A series of cases with coccidioidal pulmonary cavitation has been studied. The four representative case reports which follow are limited to patients with pulmonary cavities, residuals of the primary infection. Emphasis is placed on the residual cavity, as distinguished from residual nodular densities, because of the importance of its differentiation from other pulmonary conditions, particularly tuberculosis. From five to seven years have elapsed since these patients were exposed in the Southwest endemic area. They are generally asymptomatic and the roentgenographic appearance shows little or no change during the period of observation. The question of therapy, which has recently been mentioned prominently in the literature,[2,4] will be discussed following the case reports.

*Presented at the 15th Annual Meeting of the American College of Chest Physicians, Atlantic City, New Jersey, June 5, 1949.

**From the Thoracic Group, New York Regional Office, Veterans Administration. Published with permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the authors.

CASE REPORTS

Case 1. Cavity Mistaken for Tuberculosis: A routine roentgenogram of the chest taken prior to separation from military service in March 1946 showed "an infiltrative lesion with cavity in the apex of the right upper lobe." The patient was entirely asymptomatic. Numerous sputum and gastric examinations for acid-fast bacilli and for coccidioides immitis were negative. The intracutaneous skin test with tuberculin was positive; negative with coccidioidin and histoplasmin. The patient was discharged to his home in October 1946 with a diagnosis of pulmonary tuberculosis.

On May 11, 1948 the patient was examined on a disability compensation claim. Because he had continued in excellent subjective general health, and in view of the history of intermittent service in the New Mexico and Texas desert from 1943 to 1946, it was felt that the diagnosis should be re-evaluated. A chest roentgenogram showed an infiltration in the right upper lobe, and a cavity 2.5 cm. in diameter in the periphery of the right first intercostal space, anteriorly. Physical signs were negative except for slightly diminished breath sounds over the involved area. Smears and cultures of the sputum were negative for tubercle bacilli and for fungi. The coccidioidin test of the skin (Fig. 1) was negative in a dilution of 1:100, but it was 4 plus in a dilution of 1:10. The complement fixation test for coccidioidal infection was positive. A roentgenogram of the chest on November 8, 1948 (Fig. 2) shows no change.

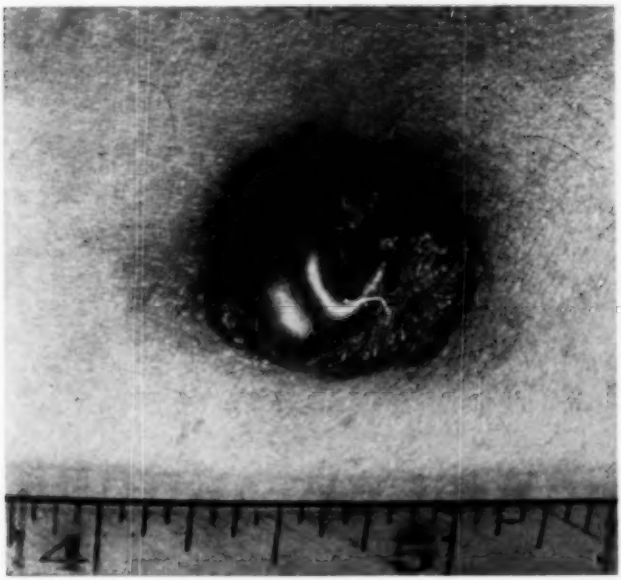

FIGURE 1: Coccidioidin skin test. Four plus reaction 24 hours following intracutaneous injection of 0.1 cc. coccidioidin, dilution 1:10 (scale in inches).

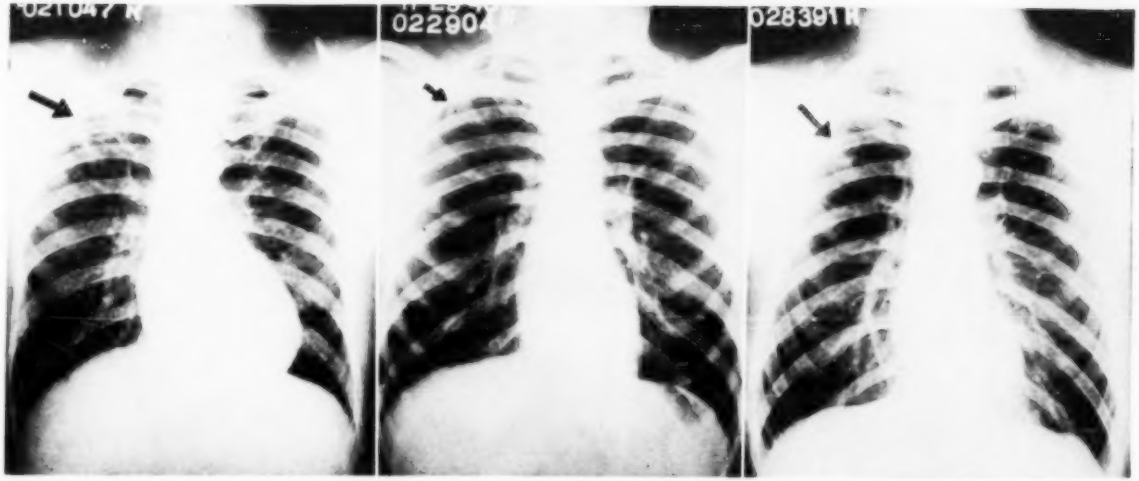

FIGURE 2 FIGURE 3 FIGURE 4

Fig. 2: Infiltration in right upper lobe. Cavity in right first intercostal space, anteriorly.—*Fig. 3:* Cavity, with no surrounding infiltration, in periphery of right upper lobe, partly hidden by second rib, anteriorly.—*Fig. 4:* Solitary cavity 2 cm. in diameter in right upper lobe.

Case 2. Solitary Cavity: In February 1945, two years after he was discharged from the Army, the patient applied for disability compensation for rheumatic heart disease. A roentgenogram of the chest disclosed a thin walled cavity, with no surrounding disease, in the upper lobe of the right lung. He was hospitalized with a tentative diagnosis of pulmonary tuberculosis. The only complaint was moderate fatigue. Sputum and gastric washings failed to reveal tubercle bacilli and he was discharged in six months.

On March 18, 1946 a chest roentgenogram demonstrated persistence of the cavity and the patient was admitted to a Veterans Administration tuberculosis hospital. Additional history of several months military service in 1942 in the Western Texas desert was noted, at which time he suffered a febrile illness accompanied by a skin eruption described as erythema nodosum. Tuberculin and coccidioidin tests of the skin gave positive reactions. Smears and cultures of gastric washings were again found negative for tubercle bacilli and fungi. Right phreniclasia was performed in March 1947 with failure to obliterate the cavity. The patient was discharged with a final diagnosis of pulmonary coccidioidomycosis "based on the characteristic x-ray appearance, negative findings for tubercle bacilli and positive coccidioidin skin test."

The chest roentgenogram on November 29, 1948 (Fig. 3), shows the cavity to be still present, almost four years since its original demonstration, with the cavity wall slightly thicker and more irregular. The coccidioidin skin test is still positive. The patient has no complaints.

Case 3. Isolated Thin Walled Cavity: In March 1948, upon learning that his sister-in-law had pulmonary tuberculosis, the patient had a roentgenogram of his chest. He had no symptom other than a mild, dry morning cough. The roentgenogram revealed a cavity in the upper lobe of the right lung, and rest in bed was advised. Gastric washings were found negative for acid-fast bacilli.

The patient was asymptomatic when he entered a Veterans hospital in July 1948. There was a history of service in the Mohave desert for three months in 1943, but no recollection of illness during that period. Examination of the chest was negative, and the remainder of the physical examination was noncontributory. Sputum and gastric washings, and also bronchoscopic washings of the right upper lobe bronchus, were negative for acid-fast bacilli and for coccidioides immitis on smear and culture. The tuberculin skin test was negative in both first and second strengths. The coccidioidin skin test gave a positive reaction. The pulmonary cavity was unchanged in September 1948, when the patient was discharged from the hospital.

A service chest roentgenogram taken on October 30, 1944 was secured from the War Department and was reviewed, and the isolated cavity, a little smaller in diameter, was found to be present. A roentgenogram on January 24, 1949 (Fig. 4), reveals a cavity 2 cm. in diameter, with no surrounding infiltration, in the right first interspace, anteriorly.

Case 4. Cavity and Small Calcific Deposits: Initial hospitalization occurred in December 1944 for minor combat wounds of the back. Following a roentgenogram of the chest a diagnosis of "ill defined disease of the lungs" was made, and the patient was evacuated to a general hospital in the United States. He was afebrile and asymptomatic. A history of four months training in the Mohave desert in 1942 was obtained. The

chest roentgenogram in May 1945 showed linear infiltrations in the left first interspace and a cavity 1 cm. in diameter in the left second interspace, anteriorly. Numerous examinations of the sputum and gastric washings were negative for acid-fast bacilli. The tuberculin and the coccidioidin skin tests gave positive reactions. Serological (complement fixation and precipitin) tests for coccidioidal infection were negative. In November 1945 a growth of coccidioides immitis was cultured out of a gastric washing. The patient received a medical discharge from service. Serial roentgenograms of the chest during the one year period of hospitalization had shown no change.

At present the patient has no complaints and he has regular full time employment as a clerk. The coccidioidin skin test still gives a positive reaction. The roentgenogram of the chest on October 5, 1948 (Fig. 5), shows some thickening of the wall of the cavity, with several tiny neighboring calcific deposits; also several small calcifications in the left hilar region.

Comment

Diagnostic Criteria: A characteristic triad is common to all the cases; (1) history of residence in the endemic area, (2) a positive

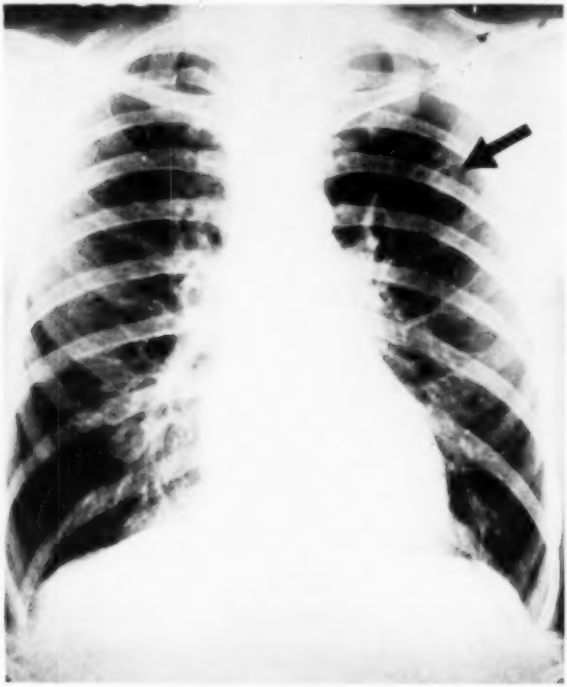

FIGURE 5: Cavity in left second intercostal space, anteriorly. Neighboring small calcific deposits.

coccidioidin skin test, and (3) persistence of residual pulmonary lesions, showing little or no change. Recovery of the etiologic fungus is not essential to the diagnosis. In only one instance (Case 4) was coccidioides immitis found. This paucity of demonstration of the etiologic agent is consistent with the fact that the majority of cases do not come under observation until several years after the onset of the infection. Worthy of note is a report by Smith[5] in which intensive efforts were made to recover the fungus in 225 cases. These cases were studied in the early stages of infection, when the fungus is more readily demonstrable, however, it was found in only 42 per cent.

Most of our cases had positive tuberculin skin tests. We do not share the reluctance of others[2] to accept the diagnosis of coccidioidomycosis in the presence of a positive tuberculin test. The benign clinical course of our patients and the practically stationary roentgen appearance of the pulmonary cavities throughout several years of observation, together with the absence of tubercle bacilli, militate against the possibility of tuberculous etiology. Coexisting pulmonary tuberculosis and coccidioidomycosis occurs occasionally; less than a dozen cases have been reported.[6] We are at present treating with artificial pneumoperitoneum a patient who developed cavitary tuberculosis subsequent to surgical resection of an upper lobe containing a coccidioidal cavity.

Therapy: Knowledge of the nature of the residual pulmonary coccidioidal lesions is essential to the intelligent application of therapeutic principles. One is at once impressed by their benignity. The lesions consist in the main of two types: (1) nodular fibrotic density and (2) cavity. Accurate figures on the overall incidence of residual cavitation are not available, but it is definitely less common than the nodule. Unlike tuberculosis, spread of the disease to the remainder of the lung fields or dissemination to distant organs rarely if ever occurs. In our patients the roentgen appearance has shown little or no change over a two to five year period of observation. The majority of cases show no symptom of illness at any time, many being discovered only on routine chest roentgenogram.

Also important in the approach to therapy is the improbability of contagion. It is generally believed that man becomes infected with coccidioidomycosis as a result of the inhalation of desert dust contaminated with chlamydospores of coccidioides immitis. A parasitic stage in the life cycle of the fungus then occurs, the fungus appearing in the human sputum as endospores. It is believed that the saprophytic stage in the soil must then occur again before the fungus can be infectious to man. Recently, however, Rosenthal and Routien[7] concluded from experiments with guinea

pigs that active primary or progressive coccidioidomycosis in humans may be contagious. In an article to be published elsewhere[5] we have reported the results of a study of 11 intimate family contacts of six patients with cavitary pulmonary coccidioidomycosis, also a contact of a patient with disseminated coccidioidomycosis. Chest roentgenograms and coccidioidin skin tests were performed after periods of two or more years of exposure. None of the contacts had become infected. The latter study, we believe, constitutes additional evidence of the noncontagiousness of the disease.

Nonintervention, therefore, should be the keystone of the therapy of these residual lung lesions. With only an occasional exception the condition is benign and the patient has few if any symptoms. Medicinal treatment is of no specific value. Collapse therapy and pulmonary resection have been and are still being performed for coccidioidal cavity. We wish to emphasize that pneumothorax or other surgical intervention is not indicated, except in the infrequent case where there is significant hemorrhage from a cavity.

SUMMARY

1) Observations on four cases with residual cavities of pulmonary coccidioidomycosis are made.

2) Diagnostic criteria and differentiation from pulmonary tuberculosis are discussed.

3) The generally benign nature of the lesions is stressed and conservative therapy is recommended.

The authors wish to express their appreciation to the Medical Illustration Unit, Bronx Veterans Administration Hospital, New York, for the photographic prints which appear in this paper.

RESUMEN

1) Ss presentan las observaciones de cuatro casos de cavidades residuales en coccidioidomicosos pulmonar.

2) Se discute el criterio diagnóstico y la diferenciación de la tuberculosis.

3) La naturaleza generalmente benigna de la lesión se recalca y se recomienda el tratamiento conservador.

REFERENCES

1 Bass, H. E., Schomer, A. and Berke, R.: "Coccidioidomycosis: Persistence of Residual Pulmonary Lesions," *Arch. Int. Med.*, 82:519, 1948.
2 Smith, C. E., Beard, R. R. and Saito, M. T.: "Pathogenesis of Coccidioidomycosis with Special Reference to Pulmonary Cavitation," *Ann. Int. Med.*, 29:623, 1948.
3 Smith, C. E., Beard, R. R., Rosenberger, H. G. and Whiting, E. G.: "Effect of Season and Dust Control on Coccidioidomycosis," *J.A.M.A.*, 132:833, 1946.
4 Krapin, D. and Lovelock, F. J.: "Recurrence of Coccidioidal Cavities

Following Lobectomy for a Bleeding Focus," *Am. Rev. Tuberc.*, 58:282, 1948.
5 Smith, C. E.: "Epedemiology of Acute Coccidioidomycosis with Erythema Nodosum ('San Joaquin' or 'Valley Fever')," *Am. J. Pub. Health*, 30:600, 1940.
6 Study, R. S. and Morgenstern, P.: "Coexisting Pulmonary Coccidioidomycosis and Tuberculosis," *New England J. Med.*, 238:837, 1948.
7 Rosenthal, S. R. and Routien, J. B.: "Contagiousness of Coccidioidomycosis: An Experimental Study," *Arch. Int. Med.*, 80:343, 1947.
8. Bass, H. E., Schomer, A. and Berke, R.: "Question of Contagion in Coccidioidomycosis: Study of Contacts," *Am. Rev. Tuberc.*, 59:632, 1949.

Discussion

ALVIS E. GREER, M.D., F.C.C.P.
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The paper presented by Dr. Berke and associates is a timely one and is a challenge to us to be on the alert for similar cases. The reported high incidence (25 per cent) of coccidioidal infection in military personnel, exposed in the southwest endemic area, does not refer to the severe forms of the disease. Most infections are relatively mild and recover promptly. Coccidioidal granuloma is infrequent, as is indicated by the health bulletins in San Joaquin Valley of California, which report an average incidence of only 46 cases of coccidioidal granuloma each year in their valley of 750,000 population.

The essayers here stressed the benignity of most of the cases. This is quite true, except for the granulomatous, progressive form, which usually occurs soon after the primary infection is acquired. Although most of the acute cases recover spontaneously, some progress into the subacute stage, wherein the bronchial and mediastinal lymph nodes frequently become involved. Beck, Traum and Harrington have observed that in infected cattle the bronchial and mediastinal lymph nodes, and these only, were involved. It seems likely that in the prolonged acute cases in the human the hilar lymph nodes are infected, may remain dormant and inactive for years, and, in some cases, be the cause of dissemination in later years.

The four cases reported today bring out some interesting facts:

1) The paucity of physical findings of the chest, although we may find depressed breath sounds, dullness and rales.
2) Erythema nodosum appearing within 5 to 21 days after the onset of the infection.
3) The tendency for the pathologic picture in the lungs to show:
   (a) Nodular lesions,
   (b) Thin-walled, cyst-like cavities,
   (c) Hilar adenopathy,
   (d) Pleural involvement, fibrosis, effusion.

There is no proof of direct man to man, or animal to man transmission of the disease. Therefore, the history of residence in a known endemic area, should suggest the possibility of coccidioidal disease in every puzzling illness. The patients do not appear to be ill. There are few subjective and objective signs. They may give a history of erythema nodosum with a concomitant arthritis, appearing some days after having a respiratory infection, usually mild, but in some cases a severe respiratory infection, frequently with some pleural pain; recovery taking place within a few weeks at the most. A latent, dormant state may persist for years, the patient may harbor a low grade, asymptomatic infection in the bronchial or mediastinal lymph nodes for many years, only to become disseminated at a later date. The clinical picture at this time is one of mild subjective complaints. The physical examination of the chest may reveal no distinctive, characteristic findings, but the negativity of evidence of tuberculosis, syphilis, tumors, other fungus diseases, should alert one to the likelihood of coccidioidal granuloma. The roentgenogram may show in individual cases only hilar enlargement, single or multiple nodular lesions of varying size within the lungs, or the characteristic thin-walled, cyst-like, cavitation. It is my opinion that persons whose past clinical histories point to previous residence for a few months in an endemic area, with negative findings of other disease, who are not seriously ill, the roentgenogram revealing a thin-walled, cyst-like cavity with little, if any, surrounding infiltration in the lungs, with a positive coccidioidin skin test and negative tuberculin, even though the mold coccidioides immites is not isolated, should be classified as cases of coccidioidal granuloma until proved otherwise. The presence of positive tuberculin reactions does cloud the diagnosis, but even so, one might be correct if the above stated symptom-complex is present, in making a tentative diagnosis of C. granuloma. The main point I wish to stress is that the diagnosis in these cases is not difficult if the physician is cognizant of its possibility.

ELLIOT P. SMART, M.D., F.C.C.P.
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This fungus has two phases, the saprophytic and the parasitic. Coccidioides immitis affects animals and humans by the inhalation of the chlamydospores and the arthrospores of the fungus, from dust of infected soil, and, as far as we know, is not transmitted from man to man, although in the recent work by Rosenthal of Chicago, there is an attempt to prove otherwise.

During the war many soldiers were known to have become infected in some of the endemic areas in which they were stationed, and their wide dispersal since has presented this disease to many localities and clinics where differentiation between it and tuberculosis is essential in selecting therapy. Sixty per cent of the cases infected in the endemic areas are asymptomatic. It is more prevalent in men than women. Women are more apt to show erythema nodosum.

The frequency of cavitation in asymptomatic coccidioidomycosis is not known. The incidence in hospital cases in the U. S. Army has been given as 2 to 8 per cent and the etiology in 274 pulmonary cavities was verified by recovery of fungus in 40 per cent and by serological tests in 49 per cent. They further report that coccidioidomycosis was not found progressive. The relatively benign nature of the cavities is indicated by the fact that in the military patients three-fifths of them were discovered incidentally. They also report that 90 per cent of the cavities were single and 70 per cent located in the upper portion of the lungs.

In diagnosing these lesions the coccidioidin skin test was the first step. The complement fixation test shows a lower titer in the pulmonary cavitations and a higher titer in the disseminated or granuloma type of disease. Dr. C. E. Smith feels that this can be used as a guide in the prognosis.

In his studies Dr. William A. Winn reported a series of cavities and he feels we should be conservative in our approach toward consideration of cavities.

I have observed a number of cases over considerable periods in the last 30 years. In the early years they were not always diagnosed and were frequently classified as cases of pulmonary tuberculosis, without finding tubercle bacilli. Prior to a proper diagnosis, and later, these cases were many times treated with pneumothorax and phrenic paralysis; also specific vaccine was used, and occasionally, where cavitation existed, pneumothorax succeeded in closure, but complications were encountered when the lesions were near the periphery, with resulting bronchopleural fistulae. Following an incident of this kind I have not continued pneumothorax treatment, except as might be indicated by specific reasons, namely, hemorrhage.

I have had no occasion to resort to any treatment, surgically or otherwise, during the last 10 years. Most of these cavities are thin-walled and found to fluctuate, becoming larger, receding, possibly disappearing, only to reappear again. Occasionally one is seen that becomes thickened with considerable fibrosis. I watched a case of this type for years, eventually to hear of her dying from pneumonia.

I feel that therapy should be divided into two groups, prophylactic and indicative, and that cavities per se, unless of such size as to encroach upon the pulmonary function or endangering the individual by hemoptysis, should be left alone. Therefore, I would stress that in the presence of cavitation of the lung, with absence of acid fast bacilli, great diligence should be observed in eliminating possibility of coccidioidomycosis.

Pulmonary Edema
Experimental Observations on Dogs Following Acute Peripheral Blood Loss*

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Opening Statement

The experiments here presented were undertaken in an attempt to seek some physiologic basis for the pulmonary edema and the pneumonia which not infrequently complicates operative procedures. One experimental approach led to another until it became apparent that we were actually investigating the physiology of hemorrhagic shock and that pulmonary edema was one of the many alterations resulting from this shock state. For this reason there will be presented in the last part of this paper a possible mechanism of hemorrhagic shock which may indeed be the mechanism of shock in its broadest sense.

The purpose of this paper is, however, to present a series of observations on dogs, which show that acute peripheral blood loss will produce pulmonary edema and pulmonary hemorrhage of marked degree. In consequence of these pulmonary changes, severe circulatory disturbance occurs in the vascular bed of the lungs. This disturbance is reflected in the circulatory system as a whole, and is quite apart from the effects of the acute blood loss. The pulmonary changes which follow bleeding are not transient; these alterations have been observed as long as four or five days. If these observations are true, and stasis in the pulmonary circulation can be anticipated as a complication of acute blood loss, then intravenous therapy in such cases must be used judiciously as to quantity and type.

The first observation was a gross specimen of right lung taken from a dog sacrificed four hours after loss of the 25 per cent blood volume. The blood loss was sustained, free-flowing from the femoral artery, using an 18 gauge needle. A cross section through the right lower lobe of the same lung quite vividly demonstrated areas of vascular congestion and hemorrhage.

In order to prove that circulatory imbalance and pulmonary stasis do exist after acute hemorrhage, the following animal ex-

*Presented at the 15th Annual Meeting, American College of Chest Physicians, Atlantic City, New Jersey, June 5, 1949.

periments in circulatory dynamics are submitted. Continuous carotid artery and pulmonary artery pressures were registered by Wiggers manometers on a moving photographic screen. Before hemorrhage the carotid artery pressure was 130/104 mm. mercury while the pulmonary artery pressure was 18 mm. mercury. During hemorrhage the carotid artery pressure began to drop and was 76/40 mm. mercury, and the pulmonary artery pressure was down to 14 mm. mercury. Twenty minutes after blood loss, the carotid artery pressure was 52/18 mm. mercury while the pulmonary artery pressure was barely perceptible. Forty minutes after blood loss, the carotid artery pressure was even lower than after 20 minutes; yet there was definite elevation of pulmonary artery pressure. Direct continuous pressures of the femoral artery, the femoral vein and the pulmonary artery were also recorded on a six-foot kymograph. This too demonstrated the plateau of elevated pulmonary artery pressure which may be anticipated 40 to 50 minutes after peripheral blood loss. There was no comparable elevation of arterial pressure. The dynamic changes here described suggest that in the face of lowered blood volume from acute blood loss there is developed a definite increase in resistance within the pulmonary vascular bed.

Pulmonary Moisture

The changes in circulatory dynamics were striking, and simultaneous pulmonary histologic studies were so convincing of associated edema that it seemed desirable to show by some quantitative procedure just when and to what extent pulmonary moisture occurs following hemorrhage. A series of animals was subjected to hemorrhage (25 per cent blood volume) and sacrificed at varying intervals after bleeding. Pulmonary moisture content was ascertained by a 72 hour desiccation and dehydration of lung samples, using the method described by Elman. In this series of 31 animals it was found that there was an initial rise of pulmonary moisture in the first 20 minutes period following hemorrhage. Forty-five minutes after blood loss, the moisture content of the lungs dropped below normal levels. A second rise of lung moisture occurred one and one-half hours after blood loss, rising to well above "normal" levels, after which the moisture gradually leveled off to average normal at four hours.

With this much evidence of tissue and alveolar edema developing following acute peripheral blood loss, it seemed wise to make hematocrit and plasma protein determinations during the same time intervals. A great many dogs of all experiments were used with uniform results. The hematocrit concentration was initially elevated at 10 minutes, reached its peak at 45 minutes, and re-

ceded to normal level or below at four hours. The plasma proteins were correspondingly depressed.

Lymph Flow

That the occurrence of pulmonary edema following hemorrhage is of sudden onset and of some severity may be graphically shown by the following experiments. The pulmonary lymphatic duct was canalized in anesthetized dogs, using the technique of Drinker. A doubling in volume of lymph flow was noted 45 minutes following hemorrhage, gradually returning to normal. This increase in lymph flow from the pulmonary lymphatic duct was paralleled by cervical systemic flow. In passing, I should state that the flow of lymph from the pulmonary lymphatic duct was greatly increased when intravenous physiologic saline was used as therapy following acute blood loss, and that there was minimum to no increase when blood or plasma were used as intravenous therapy. The dilution of the plasma proteins by physiologic sodium chloride, and the depletion of the osmotic pressure effect which results from its use, is the probable cause of the increase in pulmonary transudation when this fluid is used as therapy.

We shall next take up the pathologic lung changes. The lung picture presented in these experiments following acute hemorrhage was most impressive. Within four hours the lungs showed a mottled surface with raised red areas varying in size. The cut surface showed areas of patchy hemorrhagic infiltration. Such areas were noted largely in the middle and lower lobes and there was generalized distribution throughout the lobes. Microscopically these lungs showed tissue and alveolar edema, vascular congestion, and occasional hemorrhage and some compensatory emphysema. (We are indebted to Doctor R. A. Moore of Department of Pathology for a rather extensive score sheet of pulmonary pathologic change.) It is to be emphasized that these rather profound pathologic alterations may persist for as long as five days, and that during this time the animals may appear to be normal; hence, functional alteration of the lungs may not become apparent in spite of extensive anatomical lesions.

Intravenous Fluids

If the foregoing facts are true, it can be easily visualized that intravenous fluid administration might produce further damage to the pulmonary vascular bed by either elevation of venous pressure or dilution of the plasma proteins or both. In fact, from experimental observations, the administration of fluids following blood loss is associated with a greater increase in pulmonary moisture than is found four hours after untreated

hemorrhage. Greater degrees of pulmonary edema are noted when infusions of physiologic sodium chloride are given than when either plasma or blood is used. Use of whole blood in infusion produces slightly less pulmonary moisture than does plasma. It then becomes strikingly apparent that the use of intravenous fluid, even under optimum conditions, must be with caution following moderate to severe hemorrhage, and careful use of such treatment is thus emphasized.

Discussion

In the light of known facts concerning pulmonary physiology, it is difficult to explain the succession of physiological phenomena noted in these experiments. It seems probable that a logical approach may be as follows:

The immediate decrease in cardiac output and events subsequent to acute blood loss are: Loss of blood volume, rapid fall in vascular pressure, slowing of the circulation (our experiments to show lengthening of the circulation time were not given in this paper). These factors together produce a sudden state of circulatory anoxia. As a result of this anoxic state, endothelium is damaged, capillary endothelium becomes more permeable, and there is rapid transudation of fluid from the vascular bed to the tissue spaces and into the alveoli. There is congestion and dilation of the pulmonary capillary bed.

With this loss of fluid from the vascular bed there is hemoconcentration and elevation of the plasma protein level. As pulmonary congestion and edema become more severe, a pulmonary block to normal circulation is produced, and as oncoming blood is impounded against a pulmonary wall of resistance the pulmonary artery pressure and peripheral venous pressure rise. This, then, I believe to be the framework of circulatory and physiologic changes following acute blood loss.

Time does not permit the detailed discussion this subject deserves, but several points should be given further explanation.

The acute pulmonary edema of the first 20 minutes following blood loss may be due to two factors not yet mentioned in this paper. The first is the increase in infra-alveolar negative pressure which results from the deep breathing associated with blood loss. In 1921, Graham, using both the dog and human lung suspended in a bell jar, showed that forceful expiration will produce pleural effusion by the squeezing effect of the respiratory effort. In 1943, Drinker found that labored breathing produces an increase in pulmonary transudation in the dog, as evidenced by increase in lymph flow from the pulmonary lymphatic duct. Heavy deep breathing is noted in the experimental animal fol-

lowing acute blood loss, and in the lymph studies just presented the flow of lymph from the pulmonary lymphatic duct is increased at the time of blood loss. It seems probable that the same factor of increased negative intra-alveolar pressure may in part be accountable for the alveolar edema so quickly developed in acute blood loss. The second factor pertains to the laws of the flow of fluids, namely, "As fluids flow through tubes, velocity is inversely proportional to the cross section, and lateral pressure is inversely proportional to the velocity." Once again, it should be pointed out that the circulation time is decreased following acute blood loss and that there is vascular congestion in the lungs. These same principles are involved in the progressive development of sacculations in varicose veins. An increase intracapillary lateral pressure would tend to force fluids out of the blood vessels and augment the sucking effect of the intra-alveolar negative pressure, and produce the early edema noted in our desiccation experiments.

The question is quite naturally raised: Why should there be the very rapid drop in pulmonary moisture 45 minutes after blood loss, as shown by the desiccation experiments? The dynamic factors just described, namely, sudden increase in intra-alveolar negative pressure and the acute slowing of the circulation noted as quick response to hemorrhage, are transient. There is at this point not too much alteration in fluid balance, plasma proteins are slightly above normal, and there is a natural flow of fluid from the tissues back to the vascular system.

However, endothelial damage has been sustained. As Blalock has said, "The length of time that the patient lives with inadequate supply of blood and oxygen to the tissues determines the alterations that are to be found in them." And as Haldane stated, "Anoxia not only stops the machine but wrecks the machinery." Gradually there is again a transudation of fluid through an endothelial structure damaged by the anoxia of acute hemorrhage. Fluid accumulates in the alveoli, the lung becomes stiffened and held in hyperinspiration, and blood is gradually impounded in the pulmonary artery against this pulmonary block. It is from one to one and one-half hours after blood loss that pulmonary artery pressure reaches its peak, and it is at this same time that the second rise of pulmonary moisture also reaches its peak.

CONCLUSIONS

From a practical therapeutic standpoint, what may be gained from the observations of these experiments? The average operative blood is not too great, and patients seem to compensate for

almost any intravenous therapy given them, but even in these individuals an occasional pulmonary edema is clinically evident and postoperative pneumonia is still not infrequent. However, the elderly and poor risk person requiring radical procedure with major blood loss may come more prominently in the category of these experiments. These individuals most certainly receive varying degrees of pulmonary endothelial damage which must be reckoned with for at least five days after surgery. Intravenous plasma or blood is a requirement for them; however, it must be given to them slowly and venous pressures must be watched. One could give their additional fluid requirement by the subcutaneous route, rather than risk dilution of the plasma proteins and lowering of osmotic pressures by the use of intravenous physiologic sodium chloride, pouring the fluid into a system which is not capable of accepting it.

Abrupt elevation of blood volume by the use of too rapid administration of intravenous fluids may damage or overwhelm the lungs and subsequently produce cardiac failure through venous overload. Dilution of the plasma protein by the use of intravenous saline, physiologic sodium chloride, lowers the osmotic pressure of circulating blood, and fluid is allowed to escape from the capillaries and to aggravate an already existing pulmonary edema.

CONCLUSIONES

Desde un punto de vista práctico, qué ventaja puede obtenerse de estos experimentos? La pérdida media de sangre en una operación no es demasiado grande y los enfermos parece que compensan bien la pérdida mediante el uso de cualquier terapéutica intravenosa, pero aún en estos individuos un edema pulmonar ocasional es clínicamente evidente y la neumonía postoperatoria aún no es poco frecuente. Sin embargo, los ancianos y los malos riesgos operatorios que requieren procedimientos radicales con pérdida importante de sangre, entran más destacadamente dentro de la categoría a que se refieren estos experimentos. Estos individuos con seguridad sufren grados variables de daño endotelial pulmonar a los que hay que encarar por lo menos durante los cinco días que suceden a la intervención. El plasma intravenoso o la sangre son requeridos para ellos; sin embargo, deben darse lentamente y las presiones venosas deben vigilarse. Se puede dar la cantidad de fluídos requeridos por la vía subcutánea más bien que arriesgar la dilución de las proteínas del plasma y hacer descender las presiones osmóticas por el uso de solución fisiológica salina, al verter líquido dentro de un sistema que no es susceptible de aceptarlo.

El repentino aumento del volumen sanguíneo por la muy rápida

administración de líquidos intravenosamente, puede dañar o sobrepasar la tolerancia del pulmón y como consecuencia producirse insuficiencia cardiaca por sobrecarga venosa. La dilución de las proteínas plasmáticas por el uso de la solución intravenosa hace descender la tensión osmótica de la sangre circulante y entonces se permite que el líquido escape de los capilares agravando así el edema pulmonar ya existente.

Pulmonary Abscess as Complication of Hiatal Hernia*

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With the advent of newer antibiotics and improved surgical procedures, the early diagnosis and prompt treatment of pulmonary abscess assumes an increased importance. Since the prognosis in this disease is closely correlated with the promptness and accuracy of diagnosis, it has become imperative for the internist and surgeon, working in close cooperation, to be thoroughly familiar with the variable and often partially concealed signs and symptoms of this entity.

The purpose and scope of this article is to review the saliant features of etiology, diagnosis, and therapy of lung abscess, and also to present a case of abscess secondary to a hiatal hernia. Lung abscess as a complication of hiatal hernia has not previously been described.

CASE SUMMARY

This 57-year-old white male entered the hospital on April 15, 1948 with a history of recurrent, right upper quadrant pain radiating to the epigastrium during the preceding four to five months. The pain usually occurred at night, or after meals, and was most evident with the patient in the prone position. It lasted two to three hours, was often followed by vomiting, and was unaffected by soda, milk, or foods.

He had a particularly severe episode of vomiting seven weeks before entry that awakened him from sleep and was accompanied by choking and marked dyspnea. Ten days to two weeks after this episode, he began running a low grade fever, occurring every afternoon and ranging between 100 and 102 degrees. He also developed symptoms of profuse sweating, weight loss of 15 pounds, marked anorexia, marked weakness, and easy fatiguability. He had no history of dental or oral infections, ingestion of foreign bodies, or previous ENT surgery.

Physical findings on entry revealed an acutely ill patient with rapid shallow respirations, moderate pallor, and showing evidence of recent weight loss. Examination of the chest revealed a decrease in expansion of the left side. There was dullness to flatness on percussion at the left base and decreased breath sounds, and voice sounds in the left base and left axillary regions. The right base showed inspiratory rales, but no changes in percussion or voice sounds. There was no tracheal or medias-

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tinal shift by physical findings. The liver was enlarged two finger-breadths below the costal margin and was moderately tender.

Laboratory studies on entry revealed RBC of 3.6 million, hemoglobin of 70 per cent, WBC of 14,800 with a differential smear showing 80 per cent polys including many young forms, sedimentation rate of 29 mm. per hour, negative serology, and normal urinalysis. Chest film on entry revealed an elevation of the left dome of the diaphragm, several horizontal linear lines of increased density above the right diaphragmatic dome, a slight shift of the mediastinum to the right, and a diffuse area of increased density in the left base, at the top of which appeared a ring-like area of increased density with a light center.

Two days after entry the patient had an episode of severe vomiting, coughing, and developed marked dyspnea together with a spiking temperature of 103.4 degrees. Physical findings several hours later revealed numerous ronchi and rales in the right base, and inspiratory rales in the left base above an area of decreased breath sounds with dullness to percussion. Following this episode temperature was 103.4 degrees, pulse 160, and respirations 36. WBC at this time showed 18,000 with 92 per cent neutrophiles. Urinalysis showed 2.5 per cent sugar and no acetone. Chest film revealed a mottled increased density in the right base suggestive of pneumonitis, and an increased density in the left base, also suggestive of pneumonitis—the previously described cavity had now disappeared. The patient was placed on large doses of penicillin and sulfonamides at this time. For the following two weeks he received 60,000 units of penicillin every three hours and one gram of sulfadiazine every four hours with an initial dose of four grams. At the end of the two week period the dose of penicillin was increased to 200,000 units every three hours, and the dose of sulfadiazine was increased to 1.5 grams every four hours. Chest films revealed a persistence of the pneumonic area in both the right and left base with evidence of pleural effusion in the left base. Urinalyses continued to show 3 to 4 per cent sugar with no acetone, and a fasting blood sugar showed 225 mg. per cent. The liver enlarged to four finger-breadths below the costal margin and was tender. Liver function tests revealed four plus cephalin flocculation in 24 hours, a thymol turbidity of eight units, albumin-globulin ratio of 2.2 to 3.7, and prothrombin time of 55 per cent. Sputum studies on entry revealed a predominance of gram-positive cocci.

The patient's course was stormy, but improvement was progressive and continual. He received the previously mentioned doses of penicillin and sulfonamides for a period of three months and during this time maintained a blood sulfonamide level ranging between 13 and 17 mg. per cent. He also received aerosol penicillin therapy for the first month, but because of an allergic reaction manifested by hoarseness, laryngitis, and soreness of the mucous membranes the aerosol penicillin was discontinued. At the end of the first month he received a course of intratracheal penicillin three times weekly for an additional 30 days. The diabetic condition cleared fairly rapidly on insulin and diet and at the end of three weeks diet alone sufficed. The hepatic enlargement and abnormal liver function tests persisted during the first two months of hospitalization; then gradually began returning to normal without any specific therapy for this condition. At the end of three months the thymol turbidity was three units, cephalin flocculation was negative, urinary urobilinogen was normal, and albumin globulin ratios showed a ratio of 4.2 over 3.0.

Throughout his three months' course he continued to bring up large amounts of purulent foul sputum. He became afebrile at the end of 28 days of therapy and his symptoms after that time were persistent cough with expectoration, marked weakness, anorexia, and a dull aching pain in the lower left chest region. The right upper quadrant pain radiating to the epigastrium, which had been a principal symptom prior to entry.

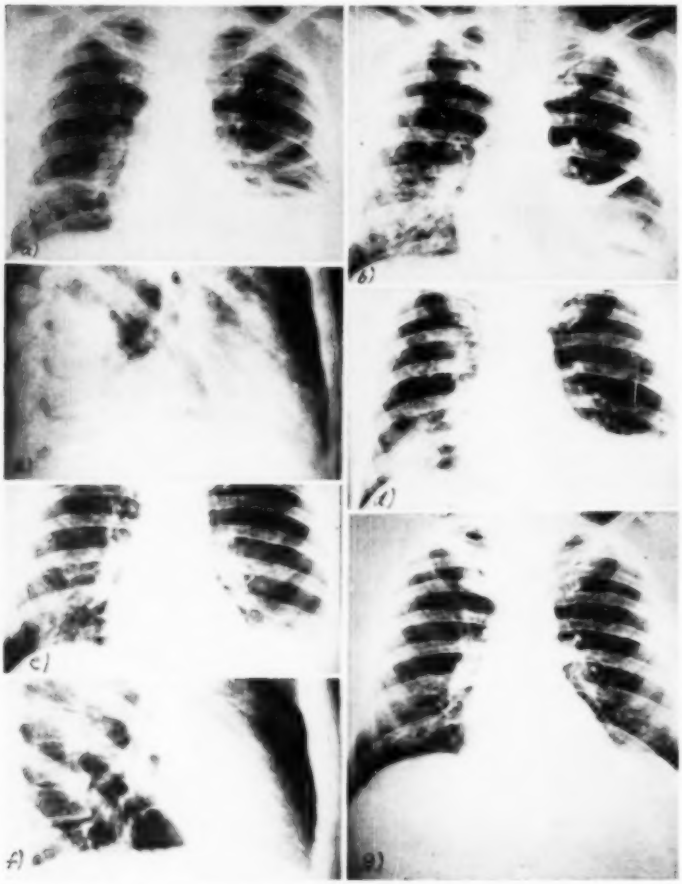


FIGURE 1: (a) X-ray film of chest taken April 15, 1948 showing evidence of walled-off abscess in left lower lung together with band-like atalectatic areas in the lower right lung.—(b) Film made April 19, 1948 following rupture of abscess with development of pneumonic areas in both lower lung fields.—(c) Left lateral view, April 29, 1948 showing pneumonitis and suggestion of abscess site.—(d) Film made May 19, 1948 showing beginning resolution of pneumonic areas.—(e) Film made June 29, 1948 showing continued resolution.—(f) Left lateral view August 29, 1948 showing clearing of pneumonitis.—(g) Film of chest August 24, 1948 showing almost complete reversal to normal.

was not apparent throughout his hospital course. Gastro intestinal series taken shortly before entry demonstrated a large hiatal hernia. The patient was bronchoscoped every two weeks for the first 10 weeks and the edematous lining of the bronchial lumen was reduced with adrenalin. Repeated sputum studies for tuberculosis including smear culture and guinea pig inocculation were negative. Repeated stool studies for amoebae were negative, and amebic complement fixation test was negative.

At the end of 90 days' therapy the patient still had residual findings in both lungs by physical findings, but was asymptomatic and afebrile. He was discharged on July 15, 1948, with residual thickened pleura in the left base, normal blood count, urinalysis, liver function tests and a sedimentation rate of 10 mm. per hour. Follow-up studies every two weeks thereafter for several months revealed a gradual clearing of the pulmonary process with no recurrence of symptoms.

In consideration of the pathogenesis of the lung abscess in this case, we shall postulate that during the episode of vomiting, coughing, and regurgitation of stored material from the hernia, some material was aspirated into the lung. This is borne out by the finding of areas of plate-like atalectasis on the entry chest film which probably arose from the plugging of small bronchi at the time of aspiration. Further, we may assume that one of the areas of atalectasis developed secondary infection and gave rise to a silent lung abscess manifested only by systemic signs up to the time of entry. At this time (March 15, 1948) the roentgenogram showed a circumscribed dense area with a radiolucent center at the apex of the left lower lobe. Shortly after entry, the rupture of the abscess was initiated by another episode of vomiting, coughing, and straining, and bronchogenic dissemination occurred. Pneumonic areas appeared in both lung fields and the abscess cavity was no longer evident (March 19, 1948). The appearance of foul sputum at this time further confirmed this sequence of events.

Discussion

Numerous classifications of lung abscess have been proposed depending on etiology. Rubin[1] divides pulmonary abscesses into four groups:

(1) pyemic abscesses secondary to emboli (these usually arise secondary to osteomyelitis, suppurative appendicitis, otitis media, urinary infection, bacterial endocarditis, or secondary to skin trauma.[2] These abscesses are usually multiple, bilateral, and form small lesions in the cortical portions of the lung.

(2) bronchiogenic abscesses including non-putrid, putrid, and chronic.

(3) abscesses secondary to pulmonary disease including infarction, neoplasm, or bronchiectasis.

(4) abscesses secondary to pathological processes of the thoracic wall, esophagus,[3] mediastinum, or spine.

The relative frequency of these various etiologies varies somewhat among different series. Lord and King,[4] in analyzing 210 cases, found that 117 followed surgery involving the upper respiratory tract. Valle,[5] in a series of 245 cases, found that 30 per cent were secondary to aspiration, 65 per cent secondary to pneumonia, 3 per cent secondary to a foreign body, and 1 per cent secondary to subphrenic abscess. Chester and Krause[6] found 17 out of 344 cases of lung abscess to be secondary to aseptic pulmonary infraction. Levin et al[7] stated that 23 cases of abscess occurred in a series of 550 cases of infarction. They felt that the sources of infection and abscess following infarction were the organisms present in chronically infected bronchi or in foci of the mouth or throat. Pyorrhea and carious teeth were also emphasized by Aufses[8] discussing the etiology of putrid lung abscess. Stats and Neuhof[9] in a series of 115 cases of acute putrid abscess, stated that the etiology was not apparent in 64 per cent of the cases, and they felt that aspiration of infected material from grossly diseased teeth or gums was probably responsible for many of these. Sweet[10] found that 56 per cent of abscesses followed ENT surgery.

The problem of when aspiration gives rise to lung abscess has long been the subject of controversy. Allen[11] felt that aspiration of infected material could give rise to abscess in the abscence of bronchial obstruction, but Rubin[1] stated that atalectasis, following impaction by a clot in the bronchus, must precede abscess formation. Cutler[12] pointed out in experimental work that secondary infection may be caused by the aspiration of buccal material during the night. He felt that an abscess was the result of aspiration of particular organisms superimposed on a thrombotic process in the lung. Kline and Berger[13] emphasized the importance of the buccal-pharyngeal region as a source by markedly reducing the incidence of postoperative abscess in a large series by rigid, preoperative, oral prophylaxis. Crowe[14] and Hedbloom[15] concluded that, for infection by aspiration to occur, the cough reflex must be sufficiently controlled to allow infected liquids to settle into the alveoli. However, Faulkner[16] felt that the cough reflex was inefficient and cited as evidence the fact that when lipiodol was introduced into the nares before sleep, it was found in the bronchi the following day.

The bacteriology of lung abscess may assume considerable importance both in diagnosis and prognosis. In one series Valle[5] found mixed organisms with pneumococci and hemolytic staphlococci predominating. Varney[17] stated that bacillus melaninogenicus was responsible for most putrid lung abscesses. Smith[18] felt that the

presence of fusospirachetal organisms following an upper respiratory infection was often the earliest sign of lung abscess.

Lung abscesses tend to occur in the lower lobes most commonly in a ratio of about 2 to 1, and in the right lung in a ratio of about 3 to 1. The right lower lobe is most commonly involved, the left lower lobe next, and the right upper lobe is third. About 75 per cent of abscesses originate in the periphery of the lung, since the smaller bronchioles tend to become occluded most easily. Abscesses usually arise in the apical segments of the lower lobe or the basal segments of the upper lobe; anatomically, these are the favorite sites for aspiration with the patient supine.

The diagnosis of lung abscess is often delayed because of the variable signs and symptoms which may predominate in a given case, or because an etiology has not been established in taking the history. We have previously indicated the importance of a history of vomiting during an alcoholic episode as an example. Particularly in children where aspiration of a foreign body is so often the precursor to the establishment of an abscess, a careful search both by history and laboratory methods is essential in establishing a possible etiology. In the series of more than 200 cases reported by Valle,[5] the presenting findings were cough, foul sputum, pleuritic pain, and fever. Hemoptysis was present in over one-half of the cases. Physical signs tend to be extremely variable and are largely dependent upon the size of the abscess, its location, and its proximity to the surface of the lung. Cabot[17] stated that the signs may only be those of inflammation of the lung parenchyma surrounding the abscess. Clubbing frequently occurs, particularly in abscesses which remain unresolved after many weeks, but has been reported during the third week of an abscess.

In the laboratory diagnosis of pulmonary abscess, there are again no specific diagnostic features. The presence of fuso-spirochetal organisms in the sputum in conjunction with a respiratory infection may suggest an early abscess.

In contradistinction to the usual type of putrid lung abscess described previously, State and Neuhof[9] have emphasized the existence of "walled-off" putrid abscesses without foul sputum because of complete obstruction of a bronchial segment. This type of abscess will present symptoms of a generalized toxemia without localization in the respiratory tract. Pain is an important finding in putrid abscess because it frequently shows the position of the abscess by overlying an area of pleuritis. The recurrence of pain during the course of an abscess frequently indicates pleural spread.

A chronic abscess is exemplified by periodic exacerbations of fever, chills, productive cough, and often pleuritic pain. The symptoms in this case are due to an inadequate drainage of en-

cysted pus pockets. A chronic abscess may be the result of fibrosis around the original area of suppuration, or may represent a diffuse involvement of neighboring tissues with associated fibrosis and bronchiectasis. Complications include amyloid degeneration of other organs, the occurrence of metastatic abscesses, or cardiac decompensation secondary to extensive pulmonary fibrosis.

Roentgenologic aids may be almost diagnostic at times, and on other occasions may show little or nothing such as in the case of abscesses following bland pulmonary infarction. The x-ray findings can be considered in three stages: (a) in the early stage, the x-ray appearance may closely simulate a pneumonitis except that two lobes are often involved; (b) in the pyogenic cavity stage, the x-ray may show a fluid level, and an air fluid level may be demonstrated when the abscess communicates with the bronchus; (c) the third stage may be one of resolution; the abscess may become larger and chronic with a thick-walled cavity predominating; or a large fibrous ring may be left around the entire area so that a large empty space results. In the localization of an abscess for operative intervention, the x-ray may be extremely valuable. The site of incision is usually at the roof of an abscess where it is nearest the surface, and Rabin[18] has emphasized the value of the "spot" method using radio opaque dye for the precise localization of a pulmonary abscess.

A sudden elevation of temperature during the course of an abscess should always be an indication for a careful roentgen study since this is often the result of the occlusion of a bronchus with the loss of air and collapse of the cavity. The continued accumulation of pus with no outlet results in signs of increasing toxicity. Conversely, a sudden change in the roentgen appearance with a fall in temperature and expectoration of large amounts of purulent sputum usually indicates that the abscess has ruptured into a bronchus and spontaneous drainage is occurring.

Among the most serious effects of lung abscesses are the complications to which they frequently give rise; namely, metastatic abscesses to the brain, spleen, liver, or kidney, bronchogenic aspiration with spread to the same or opposite lung, regional extension with resultant mediastinitis, pericarditis, or empyema. The latter may be of a small putrid type or may result in a pyopneumothorax with a bronchopleural fistula. Brown et al[19]felt that surgical drainage, preceded by penicillin therapy, was the treatment of choice in these cases.

The therapy of pulmonary abscesses has long been the subject of controversy and widely divergent viewpoints. Both medical and surgical methods have been in vogue at varying times, but today the basic principles of therapy embody features of both

methods. From the standpoint of the internist, medical therapy has assumed increasing importance with the development of newer antibiotic agents. Notwithstanding the newer developments in medical and surgical therapy, the overall mortality had not changed appreciably until recently. Allen and Blackman[20] in a review of 2,000 cases before 1936 found a mortality of slightly more than 34 per cent and Smith in a review of a similar number after 1936 found almost as high a mortality.

The value of a nutritious diet affording adequate calories, proteins for tissue regeneration, and vitamins, particularly C for wound healing, is well accepted. Frequent small transfusions for the anemia, which usually occurs in any long-standing abscess process, are of considerable benefit. Postural drainage is an invaluable aid in promoting drainage, but its usage is frequently abused. Postural drainage should be reserved not for the early pneumonic stage of an abscess but later when the sputum is becoming more profuse. The frequency of its use must be limited by the physical capacity of a sick patient. Frequent employment of drainage for short periods of time is superior to infrequent attempts for prolonged periods.

Bronchoscopy has an important role both in the diagnosis and treatment of lung abscess. In the early stages, it serves to establish drainage and relieve atalectasis by clearing an occluded bronchus; in the later stages it serves to maintain drainage. In addition, it is an aid in diagnosing foreign bodies or neoplasm as etiologies for the obstruction. It is usually felt to be contraindicated during hemorrhage. Allen and Blackman,[20] in a series of over 2,000 patients utilized bronchoscopy in one-third with a 61 per cent improvement rate and 20 per cent mortality; of their patients treated by surgery alone, 62 per cent improved and there was a 39 per cent mortality.

In a consideration of drug therapy, we find that the arsenicals were utilized extensively in the past two decades, and Smith[23] stated that they were most useful in the first 10 days, resulting in a 60 per cent recovery incidence in his series. The highest recovery rate from this type of treatment was reported by Kline and Berger[13] with a 68 per cent recovery incidence.

D'Ingianni[22] pointed out that sulfonamides were particularly valuable in pyogenic infections but were poor in fuso-spirochetal infections.

Reports on the use of penicillin have been quite encouraging. Smith[23] reported that 63.3 per cent of patients recovered, 16.7 per cent died, and 20 per cent developed chronic abscesses in a series treated by penicillin. Stivelman and Cavee[24] used penicillin in six cases of acute putrid lung abscesses with recovery in five patients,

and in seven cases of chronic abscess with improvement in five patients. They stated that spontaneous cure was rare averaging about 10 per cent. They administered penicillin every three hours in a dose of 25,000 units together with sulfonamides, and felt that therapy should continue until symptoms had subsided and the x-ray had returned to normal. Most clinicians today feel that the dose should be closer to 50,000 units every three hours, and many use 500,000 units daily in divided dosage. Alorcan[25] obtained good results in eight cases of acute suppuration of the lung, and he advocated penicillin instillation through a bronchoscope in some cases.

The introduction of aerosol penicillin marked a significant forward advance in the development of a method for achieving high local concentration. Although the blood level may not be any higher with this method, the local penetration appears to be better than that achieved by parenteral administration. The value of this form of therapy has been amply stressed by Segal and Ryder,[26] Vermilye,[27] and Findley and Sweet.[28] We have used 50,000 units in 1 c.c. of saline at four hour intervals as an average dose. Allergic reactions to this form of administration have been described, and we have observed one patient who developed edema of the tongue which responded to benadryl.

A newer development in the administration of penicillin has been the intra-bronchial instillation of moderate doses. The method as described by Stevenson[29] involves the instillation of 20,000 to 30,000 units of penicillin diluted in saline or a modified Ringer's solution into the trachea through a catheter or cannula after preliminary local anasthesia. Stevenson[29] and also Stitt[30] emphasized the precautions to be observed by reviewing the reactions which have been observed; namely, pontocaine sensitivity, which may be minimized by decreasing the amount used and employing the 1 per cent solution, dyspnea secondary to bronchial spasm, acute febrile episodes, and transient pleurisy. We have found the use of a curved metal catheter to be superior to that made of rubber. 30,000 to 40,000 units of penicillin has been our average dose of two-day intervals.

The drug therapy of chronic lung abscess is palliative at best. Kay and Meade[31] felt that extirpation was the treatment of choice and they reported only one death in nearly 100 cases.

The main problems which arise in a consideration of the surgical therapy of lung abscess are those of the type of surgery to be utilized in a given case and the optimal time for surgical intervention. Samson[32] felt that abscesses should be treated definitively in the acute stages before irreversible changes occur. He stated that the odor of expectorated sputum might serve as a

guide in determining the need for surgical intervention, i.e. more putrid odors suggest more anaerobes and emphasize the need for early external drainage. He felt that an abscess which ruptured into the pleural cavity required immediate external drainage and suggested that surgery should be employed after two or three weeks of medical therapy or at least before the sixth week. Samson advocated internal drainage plus bronchoscopy early and external drainage later or, if chronicity or bronchiectasis developed, resection. Iselin et al[33] treated with penicillin 27 patients of whom 19 had pneumonotomy together with penicillin. Of these 19 patients, 15 recovered and three died during the following year. Neuhof[34] treated 86 putrid abscesses with an 85 per cent recovery rate and 3 per cent mortality; his treatment was thoracotomy and drainage. He felt that surgery was indicated for subacute or chronic abscesses (those persisting at least six weeks) and he stated that the surgical treatment of localized abscesses afforded good results. Stats and Neuhof[9] felt that surgical therapy was the treatment of choice in "closed-off" putrid abscesses since these infections were usually of long duration at the time of diagnosis. Touroff and Neuhoff[35] in differentiating between putrid (anaerobic) and non-putrid lung abscesses pointed out that the latter tended to be multiple, not to have a foul odor, to respond better to medical herapy, and to be easily spread by surgery. If any surgery were required for these, resection was the method of choice. In the case of the putrid abscesses, surgical intervention was advised within the first six weeks. Lindskog[36] showed that the mortality rate for drainage ranged between 21 and 45 per cent for the period of 1921-1937 while in 1944 there was only a 7 per cent mortality in 24 resected cases. Glover and Clagett[37] have recently summarized the indications for pulmonary resection in lung abscess. They had 20 recoveries with 1 death in 21 lobectomies but only seven recoveries with 9 deaths in 16 pneumonectomies. Their indications for resection were: (1) persistent symptoms due to pathological changes secondary to open drainage; (2) multiple or multilocular abscesses; (3) abscesses with secondary surrounding changes; (4) abscesses not accessible to open drainage by virtue of their position; (5) abscesses with possible malignancy; (6) abscesses with excessive bleeding; (7) abscesses in children because of the tendency to chronicity and the development of drainage sinuses; and (8) abscesses secondary to a foreign body which cannot be removed by bronchoscopy.

In correlating medical and surgical therapy, it is generally felt that an early diagnosis is essential. The medical forms of therapy enumerated previously are indicated in the early stages, and the need and time for surgical intervention should depend upon the

response of the patient to medical management. It is generally felt that an acute abscess not responding in the first two or three weeks or not cleared by the sixth week should be treated surgically. In addition surgical management is definitely indicated for abscesses with secondary complications or in abscesses where drainage is inadequate.

SUMMARY

1) An unusual case of lung abscess arising secondary to a hiatal hernia has been presented.

2) A review of the etiology, pathogenesis, and diagnosis of pulmonary abscess has been given.

3) The present concepts of therapy have been reviewed. Penicillin administered in its various forms would seem to offer the best promise for success of any of the medical agents.

4) The indications and optimal time for surgical intervention have been emphasized.

RESUMEN

1) Se refiere un raro caso de absceso pulmonar subsiguiente a hernía del hiato esofágico.

2) Se presenta un repaso de la etiología, patogenia y diagnóstico del absceso pulmonar.

3) Se repasan los presentes conceptos terapéuticos. De todos los agentes médicos, la penicilina, administrada en sus varias formas, parece ofrecer la mejor promesa de resultados halagüeños.

4) Se han recalcado las indicaciones y el tiempo óptimo para la intervención quirúrgica.

REFERENCES

1 Rubin, E. H. and Rubin, M.: "Diseases of the Chest," *W. B. Saunders Co.*, Philadelphia and London, 1947.
2 Schwartz, J.: "Staphylococcal Abscess Due to Skin Trauma," *J. Mt. Sinai Hosp.*, 12:637, 1945.
3 Hannell, H.: "Perforation of an Esophageal Foreign Body into the Lung with Formation of Putrid Pulmonary Abscess," *J. Mt. Sinai Hosp.*, 13:4, 1946.
4 Lord, F. T. and King, D. S.: "Certain Aspects of Pulmonary Abscess from an Analysis of 210 Cases," *Ann. Int. Med.*, 8:468, 1934.
5 Valle, A. R.: "Lung Abscess," *Surg. Gyne. and Obst.*, 81:3, 1945.
6 Chester, E. M. and Krause, G. R.: "Lung Abscess Secondary to Aseptic Pulmonary Infarction," *Radiology*, 39:647, 1942.
7 Levin, L., Kernohan, J. W. and Moersch, H. I.: "Pulmonary Abscess Secondary to Bland Pulmonary Infarction," *Dis. of Chest*, 14:218, 1948.
8 Aufses, A. H.: "Multiple Simultaneous Acute Putrid Lung Abscesses," *Dis. of Chest*, 14:41, 1948.
9 Stats, D. and Neuhof, H.: "Putrid Pulmonary Abscess Without Foul Sputum," *Arch. Int. Med.*, 76:154, 1945.
10 Sweet, R. H.: "Analysis of Massachusetts General Hospital Cases of Lung Abscess from 1938 to 1942," *S. G. and O.*, 80:568, 1945.
11 Allen, D. S.: "Etiology of Lung Abscess," *Arch. Surg.*, 16:179, 1928.
12 Cutler, E. C.: "Experimental Production of Abscess of the Lung," *Am. J. Dis. Child.*, 38:683, 1929.

13 Kline, B. S. and Berger, S. S.: "Pulmonary Abscess and Pulmonary Gangrene," *Arch. Int. Med.*, 56:753, 1935.
14 Crowe, S. J. and Scarff, J. E.: "Experimental Abscess of the Lung in a Dog," *Arch. of Surg.*, 16:176, 1928.
15 Hedbloom, C. A., Jeaunides, M. and Rosenthal, S.: "Pulmonary Abscess; Experimental Study," *Ann. Surg.*, 88:823, 1928.
16 Faulkner, W. B. Jr. and Faulkner, E. C.: "Internal Drainage as a Factor in the Production of Postoperative Massive Collapse," *Am. J. Med. Sc.*, 184:370, 1932.
17 Cabot, R. C. and Adams, F. D.: "Physical Diagnosis," *Williams and Wilkins Co.*, Baltimore, 1939.
18 Rabin, C. B.: "Precise Localization of Pulmonary Abscess; The 'Spot' Method," *J. Thor. Surg.*, 10:662, 1941.
19 Brown, B., Ory, E. M., Meads, M. and Finland, M.: "Penicillin Therapy of Empyema," *Ann. Int. Med.*, 24:343, 1946.
20 Allen, C. I. and Blackman, J. F.: "Treatment of Lung Abscess with Report of 100 Consecutive Cases," *J. Thor. Surg.*, 6:156, 1936.
21 Smith, D. T.: "Diagnosis and Treatment of Fusospirochetal Type of Lung Abscess," *Internat. Cl.*, 4:221, 1936.
22 D'Ingianni, V.: "Non-tuberculous Lung Abscess; Survey of 417 Cases," *Am. J. Surg.*, 65:46, 1944.
23 Smith, D. T.: "Medical Therapy of Acute and Chronic Pulmonary Abscesses," *J. Thor. Surg.*, 17:72, 1948.
24 Stivelman, B. P. and Kavee, J.: "Penicillin in the Treatment of Putrid Lung Abscess," *Ann. Int. Med.*, 25:166, 1946.
25 Alarcon, D. G.: "Penicillin in Acute Suppuration of the Lung," *Dis. of Chest*, 13:211, 1947.
26 Segal, M. S. and Ryder, Claire M.: "Penicillin Aerosolization in the Treatment of Serious Respiratory Infections," *New Eng. J. Med.*, 233: 747, 1945.
27 Vermilye, H. N.: "Aerosol Penicillin in General Practice," *J.A.M.A.*, 129:250, 1945.
28 Findlay, A. W. and Sweet, R. H.: "Aerosol Penicillin as a Therapeutic Adjunct in the Preparation of Patients with Suppuration of the Lung for Pulmonary Resection," *J. Thor. Surg.*, 16:81, 1947.
29 Stevenson, J. P.: "Bronchial Lavage for Bronchiectasis," *Am. Rev. Tuberc.*, 56:279, 1947.
30 Stitt, H. L.: "Bronchial Lavage in Non-Tuberculous Infections," *Ann. Otol. Rhin. and Laryng.*, 52:477, 1943.
31 Kay, E. B. and Meade, R. H.: "Penicillin in the Treatment of Chronic Infection of the Lung and Bronchi; Analysis of 93 Cases," *J.A.M.A.*, 129:200, 1945.
32 Samson, P. C.: "Lung Abscess (Surgical Aspects)," *Dis. of Chest*, 14: 79, 1948.
33 Iselin, M., Sureau, B. and Desmot, R.: "Penicillin and Surgical Treatment of Pulmonary Abscess," *Presse Medicale*, Paris, 55:477, 1947.
34 Neuhoff, H., Touroff, A. S. and Aufses, A. H.: "Surgical Treatment by Drainage of Subacute and Chronic Putrid Abscess of the Lung," *Ann. Surg.*, 113:209, 1941.
35 Touroff, A. S. W. and Neuhof, H.: "Differentiation Between Acute Putrid and Non-putrid Lung Abscesses," *J. Thor. Surg.*, 10:618, 1941.
36 Lindskog, G. E.: "Surgical Treatment of Lung Abscess," *Internat. Cl.*, 1:184, 1941.
37 Glover, R. P. and Clagett, O. T.: "Pulmonary Resection for Abscess of the Lung," *S. G. and O.*, 86:385, 1948.

Semi-Annual Meeting, Board of Regents

The Semi-Annual Meeting of the Board of Regents of the College was held at the Hotel Statler, Washington, D. C., on Monday, December 5. The following Regents and invited guests attended the meeting and dinner of the Board of Regents:

Paul A. Turner, M.D., Louisville, Kentucky, Chairman
Robert J. Anderson, M.D., Washington, D. C., Governor, U. S. Public Health Service
Andrew L. Banyai, M.D., Milwaukee, Wisconsin, Regent
Benjamin L. Brock, M.D., Downey, Illinois, Acting Treasurer
Robert O. Canada, Comdr., Washington, D. C., Governor, U. S. Navy
Dean B. Cole, M.D., Richmond, Virginia, Regent
Edgar W Davis, M.D., Washington, D. C., Governor, District of Columbia
Frank R. Ferlaino, M.D., New York, N. Y., Secretary, Council on Postgraduate Medical Education
Arden Freer, M.D., Washington, D. C., Governor, U. S. Army
Carl H. Gellenthien, M.D., Valmora, New Mexico, Regent
Edward A. Greco, M.D., Portland, Maine, Regent
Alvis E. Greer, M.D., Houston, Texas, Governor
Robert H. Hayes, M.D., Chicago, Illinois, Guest
Charles M. Hendricks, M.D., El Paso, Texas, Past-President
Robert B. Homan Jr., M.D., El Paso, Texas, Regent
William A. Hudson, M.D., Detroit, Michigan, Regent
Chevalier L. Jackson, M.D., Philadelphia, Pa., Second Vice-President
Hollis E. Johnson, M.D., Nashville, Tennessee, Regent
Bernard Klein, M.D., Joliet, Illinois, Guest
Edwin R. Levine, M.D., Chicago, Illinois, Chairman Council on the Management and Treatment of Diseases of the Chest
Shelley U. Marietta, M.D., Washington, D. C., Past-President
Louis Mark, M.D., Columbus, Ohio, President-Elect
Donald R. McKay, M.D., Buffalo, New York, Regent
Jay Arthur Myers, M.D., Minneapolis, Minnesota, Past-President
Richard H. Overholt, M.D., Brookline, Massachusetts, Past-President
J. Winthrop Peabody, M.D., Washington, D. C., Past-President
Joseph C. Placak, M.D., Cleveland, Ohio, President
James H. Stygall, M.D., Indianapolis, Indiana, Regent

Murray Kornfeld, Chicago, Illinois, Executive Secretary
Harriet E. Lumm, Chicago, Illinois, Assistant Executive Secretary

The dinner meeting was addressed by Mr. William Lahey, attorney-at-law, of Washington, D. C.

Dr. Paul A. Turner called the meeting to order and the College Registration Book was signed by those present.

Dr. William A. Hudson, Historian of the College, said the following words in memory of Dr. Harry C. Warren:

"Harry C. Warren, one of the Charter Members and First Vice-President of the American College of Chest Physicians, a most gracious host whose pleasing personality pervaded the meetings of the College, loved his fellow man to such a degree that he spent his lifetime in the service of humanity. His was a devotion which endeared him to all. He gave of his material and moral self, that the world and those who knew him might be happier for his having passed this way. He was of a humble spirit and his services were offered to rich and poor alike. His memory will be engraved in the minds and hearts of all who were blessed by the touch of his kindly, solicitous and understanding ministration."

In tribute, the assembly stood in a moment of silence.

AGENDA

Dr. Paul A. Turner, Louisville, Kentucky, Chairman, presiding

Roll Call:

Report of the Treasurer,
Dr. Benjamin L. Brock, Downey, Illinois, Acting Treasurer

Report of the Membership Committee,
Dr. Chevalier L. Jackson, Philadelphia, Pennsylvania, Chairman

Report of the Editorial Board,
Dr. Jay Arthur Myers, Minneapolis, Minnesota, Chairman

Report of the Executive Secretary,
Mr. Murray Kornfeld, Chicago, Illinois

Report of the Council on International Affairs,
Dr. Chevalier L. Jackson, Philadelphia, Pennsylvania, Chairman

Report of the Council on European Affairs,
Dr. Andrew L. Banyai, Milwaukee, Wisconsin, Chairman

Report of the Council on Pan American Affairs,
Dr. Richard H. Overholt, Brookline, Massachusetts, Chairman

Report of the Council on African and Eastern Affairs,
Dr. Edgar Mayer, New York, New York, Chairman

Report of the Council on Pan Pacific Affairs,
Dr. Seymour M. Farber, San Francisco, California, Chairman

Report of the Council on Undergraduate Medical Education,
Dr. Edward W. Hayes, Monrovia, California, Chairman

Report of the Council on Postgraduate Medical Education,
Dr. J. Winthrop Peabody, Washington, D. C., Chairman

Report of the Council on Research,
Dr. Charles M. Hendricks, El Paso, Texas, Chairman

Report of the Council of Tuberculosis Committees,
Dr. James H. Stygall, Indianapolis, Indiana, Chairman

Report of the Council of Tuberculosis Hospitals,
Dr. Russell S. Anderson, Erie, Pennsylvania, Chairman

Report of the Council on Public Health,
Dr. Robert J. Anderson, Washington, D. C., Chairman

Committee Reports

Resolutions

Communications

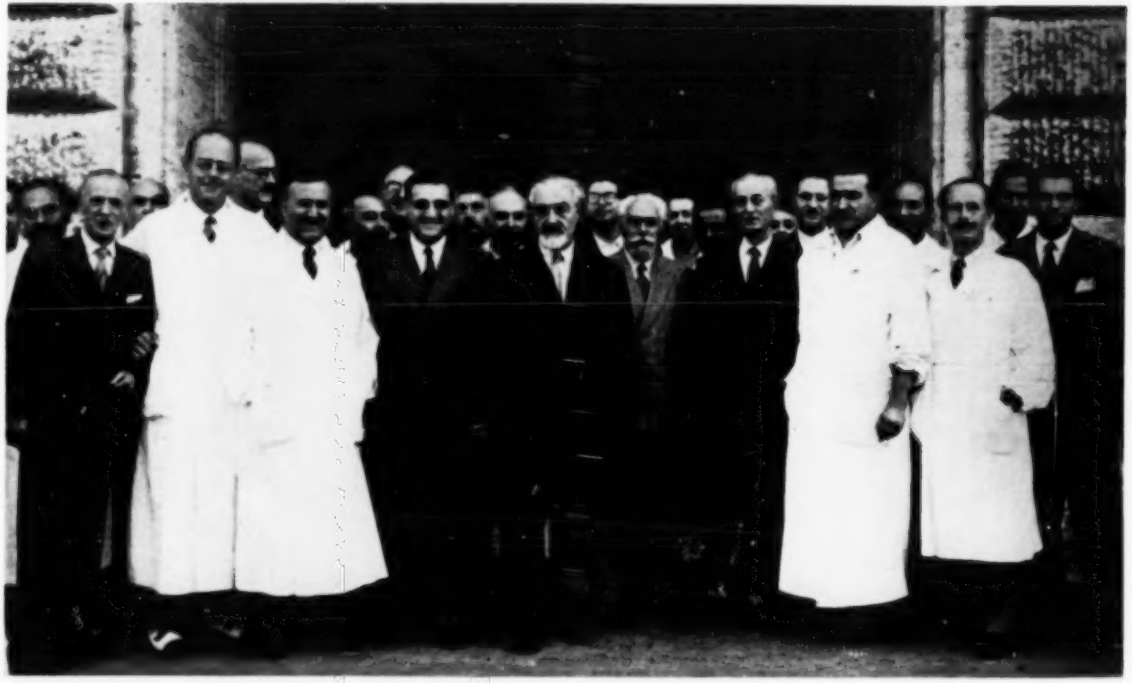
New Business

Adjournment

First International Congress on Diseases of the Chest

Plans have been completed for the First International Congress on Diseases of the Chest to be held at the Forlanini Institute, Rome, Italy, September 17-20, 1950. The Congress will be sponsored by the Council on International Affairs of the American College of Chest Physicians and the Forlanini Institute. Mr. Murray Kornfeld, the Executive Secretary of the College, recently returned from Europe where he met with Fellows of the College and other officials in Italy to make the necessary arrangements for the Congress. Professor Eugenio Morelli, Professor of Tuberculosis at the medical school, and Professor A. Omodei Zorini,

GROUP MEETS TO PLAN THE FIRST INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST



Photograph taken in front of the Carlo Forlanini Institute, Rome Italy, September 21, 1949. First row, standing from left to right: Dr. Cesari, Professor Fegiz, Professor Omodei Zorini, Mr. Murray Kornfeld, Professor Morelli, Professor Ficacci, Dr. Ronco, Professor L'Eltore, Professor Daddi, and Dr. Romeyn.

Medical Director of the Forlanini Institute, are the co-chairmen for the Congress, and Professor Giovanni L'Eltore, Assistant Director of the Forlanini Institute and Secretary General of the Italian Federation Against Tuberculosis, is in charge of hotel accommodations.

Mr. Kornfeld reports that there will be a large pilgrimage to Rome in 1950 for the Holy Year and that the capacity of the hotels will be taxed to the utmost. Physicians who wish to attend the Congress should, therefore, write at once to Professor L'Eltore for hotel reservations and a copy of the communication should be sent to the Executive Secretary of the College in Chicago. For further information please refer to front advertising page number x of this issue of the journal.

Requests for places on the program should be directed to the Council on International Affairs of the American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois, U.S.A.

The meeting to inaugurate the plans for the Congress was held at the Forlanini Institute in Rome on September 21, 1949 and the meeting was addressed by Professor Zorini, Professor L'Eltore and Mr. Kornfeld. Approximately 100 physicians attended this meeting. The final plans for the Congress were approved at a meeting in Montecatini, Italy on October 26, 1949.

The Congress has been approved by the Department of Public Health of Italy, Professor Mario Cotellessa, Minister of Health; the Department of Foreign Affairs of Italy, Dr. Andreotti, Assistant Secretary of State; and the National Institute of Health, Mr. Angelo Corsi, President.

Communications have been received at the Executive Offices from College officials in more than twenty countries, expressing their interest in the Congress and stating that their countries will send delegates.

While in Europe, Mr. Kornfeld also visited with College officials and members in Switzerland, England, France, Holland, Belgium, Spain and Portugal. Plans for the expansion of College activities in these countries were discussed as well as their participation in the First International Congress on Diseases of the Chest to be held in Rome, September 17-20, 1950.

World Medical Association

The American College of Chest Physicians was represented at the meeting of the World Medical Association held in London, England, October 10-15, 1949. The meeting was concerned with the establishment of an international code of medical ethics and a report of the committee on postgraduate medical education was discussed. The reports made by representatives of the World Health Organization, UNESCO, the International Labor Office, and the International Red Cross were also received and discussed by the Congress. The meeting was presided over by Dr. Charles Hill of Great Britain, the President of the World Medical Association. Dr. Elmer L. Henderson, of the United States, is the President-Elect and will preside at the next meeting of the Association to be held in New York City in 1951. Dr. T. C. Routley of Canada serves as Chairman of the Council, Dr. Louis H. Bauer, United States, Secretary-General, and Dr. Morris Fishbein, United States, is the Editor of the Bulletin. Delegates from 27 countries were represented at the Congress.

POSTGRADUATE COURSE IN DISEASES OF THE CHEST, AMERICAN COLLEGE OF CHEST PHYSICIANS
November 14-18, 1949, Hotel New Yorker, New York City

Some of the physicians and instructors who participated in the Postgraduate Course in Diseases of the Chest of the American College of Chest Physicians.

Postgraduate Course Held in New York City

The Council on Postgraduate Medical Education and the New York State Chapter of the American College of Chest Physicians sponsored a postgraduate course in diseases of the chest which was held at the Hotel New Yorker, New York City, during the week of November 14-18, 1949. Dr. Edgar Mayer, New York City, served as chairman of the postgraduate course, and Dr. Frank R. Ferlaino, also of New York City, served as secretary. The total number of physicians registered for the course was 86. A photograph of the group taken during the course appears on the opposite page.

On Sunday, November 13, the day before the course opened, Dr. and Mrs. Edgar Mayer entertained the registered physicians and the faculty at a cocktail party in their home in Tarrytown, New York.

College Chapter News

ILLINOIS CHAPTER

The Illinois Chapter of the College held a meeting on Friday, December 9, 1949, at the Congress Hotel, Chicago, at which the following program was presented:

"Surgical Treatment of Giant Lung Cysts and Emphysematous Bullae,"
Jerome R. Head, M.D., F.C.C.P., Chicago.

Discussants: David F. Loewen, M.D., F.C.C.P., Decatur, and Edward Avery, M.D., Hines.

"Indications and Results of Lung Excision in Tuberculosis,"
S. Allen Mackler, M.D., F.C.C.P., Chicago.

Discussant: Jesse A. Stocker, M.D., F.C.C.P., Springfield.

NEW YORK STATE CHAPTER

The annual meeting of the New York State Chapter of the College will be held at the Hotel New Yorker, New York City, on Thursday, February 16, 1950. The following program will be presented:

Morning Session:

David Ulmar, M.D., F.C.C.P., chairman.

"Fluoroscopic Anatomy of the Heart,"
Martin M. Maliner, M.D.

"Cardiac Pathology as Discovered on Routine Mass Chest X-ray Surveys,"
Hyman Alexander, M.D.

"Angiography in Cardiac Visualization,"
George Porter Robb, M.D.

Discussants: Henry K. Taylor, M.D. and Robert McGrath, M.D.

Luncheon:

Joseph J. Witt, M.D., F.C.C.P., President, New York State Chapter, American College of Chest Physicians, presiding.

Guest Speaker: Herbert R. Edwards, M.D., Executive Director, New York Tuberculosis and Health Association,
"The Significance of Tuberculosis Today."

Afternoon Session:

Edgar Mayer, M.D., F.C.C.P., chairman.

"Respiratory Effects of Volatile Substances,"
A. G. Cranch, M.D. and T. W. Nale, M.D.

"Dust Inhalation in Relation to Pulmonary Disease,"
Leonard Greenburg, M.D.

"Alterations in Pulmonary Physiology Produced by Inhalation of Harmful Substances,"
Richard L. Riley, M.D.

Discussants: A. J. Lanza, M.D. and L. J. Goldwater, M.D.

Dinner:

Joseph J. Witt, M.D., F.C.C.P., President, New York State Chapter, American College of Chest Physicians, presiding.

Guest Speaker: Joseph C. Placak, M.D., Cleveland, Ohio,
President, American College of Chest Physicians.

PENNSYLVANIA CHAPTER

The Pennsylvania Chapter of the College met at Devitt's Camp, Allenwood, Pennsylvania, on October 22, 1949. The following papers were presented:

"The Management of Tension Cavities in Tuberculosis,"
John S. Packard, M.D., F.C.C.P., Allenwood.

"Treatment of Pulmonary Tuberculosis with Pneumoperitoneum,"
Elmer R. Hodil, M.D., F.C.C.P., Allenwood.

"Treatment of Tuberculosis with Para Aminosalicylic Acid,"
Howard E. Stine, M.D., Allenwood.

"Tuberculosis of the Larynx with Response to Streptomycin,"
William A. Lell, M.D., Philadelphia.

"After Resection, What More can Surgery do for Pulmonary Tuberculosis?"
Charles P. Bailey, M.D., F.C.C.P., Philadelphia.

"Lipiodol Study of a Blocked Cavity,"
John T. Szypulski, M.D., F.C.C.P., Mt. Carmel.

"X-ray Case Reports,"
Royal H. McCutcheon, M.D., F.C.C.P., Bethlehem.

At a business meeting of the chapter, the following officers were elected for the coming year:

Edward Lebovitz, M.D., Pittsburgh, President.
Archibald Judd, M.D., Hamburg, First Vice-President.
Victor M. Leffingwell, M.D., Charon, Second Vice-President.
John V. Foster, M.D., Harrisburg, Secretary-Treasurer.

College News Notes

The following members of the College participated in the program on Diseases of the Chest presented at the Clinical Session of the American Medical Association held in Washington, D. C., December 6 through 9, 1949: Drs. Andrew L. Banyai, Leon H. Hirsh, Edwin R. Levine, Martin J. Sokoloff, Alvan L. Barach, Jay Arthur Myers, Robert J. Anderson, Edgar W. Davis, Maurice S. Segal, Louis L. Friedman, Hyman E. Bass, A. Worth Hobby, Edgar Mayer, Oscar A. Sander, and Osler A. Abbott. Drs. Chevalier L. Jackson and Daniel L. Finucane presented papers in the Session on Pediatrics.

Dr. Jay Arthur Myers was presented with a plaque for distinguished service in tuberculosis control by the Minnesota Public Health Association, October 25, 1949 on the occasion of the publication of his latest book "Invited and Conquered," a history of tuberculosis in Minnesota.

Dr. Phillip Cohn, Chief of Staff of the Southern Indiana Tuberculosis Hospital, New Albany, Indiana, has been elected President of the Floyd County Medical Society for the year 1950.

Dr. Juan R. Herradora, Secretary of the Council on Pan American Affairs of the College, recently visited Cordoba, Argentina, as an official delegate of the College from the United States of America to the Second Argentine Congress on Tuberculosis, November 28-30, 1949, and also attended the Annual Meeting of the Argentine Chapter of the College which was held in the city of Rosario. Dr. Gumersindo Sayago, Regent of the College for Argentina, served as President of the Second Argentine Congress of Tuberculosis. En route to and from the Congress, Dr. Herradora visited with the following officials in other countries in South America: Dr. Orrego Puelma, Santiago, Chile; Dr. Ovidio Garcia Rosell, Lima, Peru; Dr. Fernando Gomez, Montevideo, Uruguay; and Dr. Jorge Higgins, Guayaquil, Ecuador.

At the meeting of the American Society of Anesthesiologists held at the Hotel New Yorker, New York City, on December 8, 1949, Dr. Samuel A. Thompson presented a paper on "Problems in Thoracic Surgery," in a symposium on anesthesia.

Dr. Andrew L. Banyai of Milwaukee, Wisconsin, lectured in the postgraduate course on diseases of the chest presented in San Francisco, December 5-9, 1949 under the sponsorship of the College. En route home, he visited in Los Angeles and lectured at the Birmingham Veterans Hospital, Van Nuys, and the Cedars of Lebanon Hospital in Los Angeles.

Dr. Peter J. Galante, Chief, Professional Services, Veterans Administration Center, Whipple, Arizona, spoke on October 15, 1949 to the Arizona State Tuberculosis Association in Phoenix on "Chemotherapy in Tuberculosis."

Dr. Leo V. Schneider, Chief, Tuberculosis Control Section, Veterans Administration Tuberculosis Division, addressed the general session of the Southern Tuberculosis Conference in Memphis, Tennessee, September 15, 1949 on the subject "The Place of Veterans Problems in Tuberculosis Control."

The monthly medical meeting of the Surgeon General, Department of the Army, was held Thursday evening, October 20, 1949 at Sternberg Auditorium, Army Medical Center, Washington, D. C. The subject of this meeting was "Recent Advances in the Treatment of Pulmonary Tuberculosis" which was presented by Colonel Carl W. Tempel, MC, Chief of the Tuberculosis Branch at Fitzsimons General Hospital, Denver, Colorado. This was followed by a discussion by Dr. Esmond R. Long, Director of the Henry Phipps Institute, Philadelphia, Pennsylvania, and consultant on tuberculosis to the Surgeon General.

HARRY C. WARREN, M.D., F.C.C.P.

1881 - 1949

Harry C. Warren

A Tribute

He was born 68 years ago in the town of Winnemucca, Nevada, where he received his early schooling. In 1904 he graduated from Toland Medical School, now University of California, and interned at the Marine Hospital in San Francisco. After his internship, he practiced for a short time in San Francisco and then worked in a lumber camp at Duncan Mills. He would speak often of his wonderful experiences at the latter place where he worked 24 hours a day, often operating by lamp light. In 1906, he opened an office in San Mateo County where he practiced general medicine. But even at that early date, he became interested in the prevention and control of tuberculosis. It was here that he met Dr. Max Rothschild, with whom he opened, in 1910, the California Sanitarium, an association which blossomed into a real Damon and Pythias friendship. This friendship persisted until Max Rothschild's death in 1936 but was then transferred to his family. This friendship was the great highlight of Harry's life. Between these two men, it was always one for all and all for one. Together, they did probably the first artificial pneumothorax ever performed in California in the year of 1910. Under their joint ownership, the California Sanitarium prospered and became the largest private institution for the treatment of chest disease west of Chicago.

Another friendship formed early in life was that between Harry Warren and Charles S. Howard, Buick automobile representative at the time for the Pacific Coast. The present Charles S. Howard Foundation for rheumatic children, located in a separate building on ground given by the California Sanitarium, cares for 22 rheumatic children and is entirely endowed and operated by the Howard family. Initially, it was supposed to care for undernourished children. This gift was due to a friendship started between two men early in their lives and continued until the death of one of them. The Howard Foundation will continue not only as a memorial to its founder, but as a great tribute to Harry Warren.

Not only did he succeed in his profession beyond perhaps his own dreams, but he found time to do work as a citizen and altruist. He devoted much time to improving health conditions in San Mateo County. He was at one time president of the San Mateo Tuberculosis and Health Association and only the year before his death was president of the California Tuberculosis Association. His influence as a tuberculosis authority, scientifically and in the prevention of the disease, was equal to that of any person in the field.

Unfortunately, his untimely death has prevented him from becoming president-elect of the American College of Chest Physicians, an organization which he not only helped establish but to which he gave much of his time and substance. He loved this organization very much and the last day of his life expressed regret that he could not live to accept the highest honor it had to give.

So much for the facts of Harry Warren's successful career as doctor, citizen, and businessman. There is, however, something very much more important to be said about him; heart and character do not always go along with mind, ability, and energy. It did, however, in this man.

He was modest and self-effacing to a fault so that few knew his inner workings. He was not only the meticulous doctor to his great host of patients, he was their close friend. He verily gave his life out of devotion and friendship to many of his patients whom he had known and served for nearly 50 years. He was a friend to his friends because loyalty and friendship meant more to him than material gain. His passing will leave a great void in his family midst, but it will leave just as great a void in the hearts and memories of his patients and friends. Truly it can be said of him "Greater love hath no man than this: That a man lay down his life for his friends."

William C. Voorsanger, M.D.

Samuel Jerome Hurwitt

1893 - 1949

Dr. Samuel Jerome Hurwitt of San Francisco, passed away on June 5, 1949 after an illness of three years. He was born in New York City and was 56 years old at the time of his death. He graduated from the University of Kansas School of Medicine in 1921. He has been a member of the San Francisco County Medical Society since 1928 and practiced medicine in San Francisco for over twenty years with offices in the Flood Building.

He had been consultant in Diseases of the Chest at the University of California Chest Clinic since 1943. Dr. Hurwitt was particularly interested in social welfare and was active in tuberculosis control work in the San Francisco Department of Health.

In addition to being a member of the San Francisco County Medical Society he was a member of the California Trudeau Society, Laennec Society, American Trudeau Society and the American College of Chest Physicians.

He is survived by his wife, Esther.

Buford H. Wardrip, M.D., Governor for California.

COURSES IN BRONCHOESOPHAGOLOGY

The University of Illinois, College of Medicine, announces a winter and spring postgraduate course in Bronchoesophagology which will be supervised by Doctors Paul Holinger and Albert Andrews.

These courses will be held from February 13 through February 25, 1950 and May 29 through June 10, 1950. For application forms and further information communicate with the Department of Otolaryngology, University of Illinois, 1853 West Polk Street, Chicago 12, Illinois.

Medical Service Bureau

POSITIONS AVAILABLE

WANTED IMMEDIATELY: Assistant staff physician for tuberculosis hospital in Hawaii. Entirely new, 200-bed institution now being built. Salary for appointee with two years previous institutional training $6,780-$7,980 in addition to fully furnished home. Non-competitive Civil Service appointment with Retirement benefits, annual vacation and sick leave. Must be citizen of the United States and graduate of United States or Canadian Medical School. Woman eligible. Ability to administer pneumothorax and read x-rays essential. Knowledge of major chest surgery not necessary. Apply with all pertinent information and recent photo to Box 203A, American College of Chest Physicians, 500 N. Dearborn St., Chicago 10, Ill.

Physician wanted for tuberculosis hospital in Texas, eligible for Texas license. Some experience in tuberculosis preferred. Salary $4,500 per year with full maintenance for a single man. Please address Box 204A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

Staff physician or resident wanted for approved tuberculosis hospital; some experience in tuberculosis necessary. Indiana license required. Modern hospital, complete diagnostic and therapeutic facilities, social, rehabilitation and out-patient services. Salary $7,200 per year plus maintenance for a small family in newly built apartment. Please address Box 205A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

Position open for Assistant Medical Director for 225 bed tuberculosis hospital. Salary $4,800 a year, with full maintenance and a furnished house on grounds Will consider male or female physician who has one, two, or more years experience in tuberculosis. Write to Dr. A. J. Viehman, Medical Director, Jefferson Tuberculosis Sanatorium, Route 2, Birmingham 9, Alabama.

Physician wanted for tuberculosis hospital in Northwest. Some experience in diagnosis and treatment of tuberculosis desired. Surgical work available. Starting salary $415.00 per month plus complete maintenance including house, increase in six months. For further information please address Box 206A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

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A modern, thoroughly equipped institution for the treatment of tuberculosis. Located on a large 350-acre farm in the beautiful, healthful Maryland countryside. All city conveniences . . . eight miles north of Baltimore . . . one mile east of Towson, Maryland.

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A thoroughly equipped institution for the modern medical and surgical treatment of tuberculosis. An especially constructed unit for thoracic surgery. The most recent advances in pneumolysis applied to those cases demanding this branch of intrathoracic surgery.

MODERATE RATES

Descriptive Booklet on Request

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